

L10 ANSWER 2 OF 3 MEDLINE
ACCESSION NUMBER: 95333876 MEDLINE
DOCUMENT NUMBER: 95333876
TITLE: Cholesteryl ester transfer protein inhibition in hypercholesterolemic hamsters: kinetics of apoprotein changes.
AUTHOR: Zuckerman S H; Evans G F
CORPORATE SOURCE: Division of Cardiovascular Research, Lilly Research Labs, Indianapolis, Indiana 46285, USA.
SOURCE: LIPIDS, (1995 Apr) 30 (4) 307-11.
Journal code: L73. ISSN: 0024-4201.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
AB Inhibition of cholesteryl ester transfer protein (CETP) activity in hypercholesterolemic hamsters results in elevated high-density lipoprotein (HDL) cholesterol, an increase in HDL size, and the appearance of apolipoprotein E (apo E)-rich, apo A-I-poor particles. The present study has focused on the kinetics of apoprotein redistribution among the HDL particles and the relative increase in HDL-associated apo E and CETP in hypercholesterolemic hamsters, following inhibition of transfer activity using the monoclonal antibody, TP2. A 60% inhibition in CETP activity was observed 24 h after antibody injection and was associated with an increase in HDL cholesterol and HDL size. Increased amounts of apo E were associated with these HDL particles and remained in this fraction throughout the duration of the study. In contrast, while CETP was also detected on large HDL particles, this distribution shifted back toward the pretreatment pattern by 14 d. The dynamic changes in apoprotein distribution may represent a compensatory physiologic response following disruption of reverse cholesterol transport.

L10 ANSWER 3 OF 3 MEDLINE
ACCESSION NUMBER: 95105666 MEDLINE
DOCUMENT NUMBER: 95105666
TITLE: Inhibition of cholesteryl ester transfer protein in normocholesterolemic and hypercholesterolemic hamsters: effects on HDL subspecies, quantity, and apolipoprotein distribution.
AUTHOR: Evans G F; Bensch W R; Apelgren L D; Bailey D; Kauffman R F; Bumol T F; Zuckerman S H
CORPORATE SOURCE: Division of Cardiovascular Research, Lilly Research Labs, Lilly Corporate Center, Indianapolis, IN 46285..
SOURCE: JOURNAL OF LIPID RESEARCH, (1994 Sep) 35 (9) 1634-45.
Journal code: IX3. ISSN: 0022-2275.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
AB The effects of cholesteryl ester transfer protein (CETP) inhibition on the serum lipoprotein profile in both normocholesterolemic and hypercholesterolemic hamsters has been determined following subcutaneous injection of 12.5 mg/kg of the CETP neutralizing monoclonal

antibody, TP2. Inhibition of CETP activity was greater than 60% and resulted in a 30-40% increase in high density lipoprotein (HDL) in both normal and hypercholesterolemic animals. These HDL effects were observed

1 day post-injection, were maximal by 4 days, and returned to control values

by 14 days. Inhibition of CETP activity resulted in a decrease in both low

density lipoprotein (LDL) and very low density lipoprotein (VLDL) cholesterol concomitant with HDL increase, and in hypercholesterolemic animals resulted in increased total serum cholesterol. In addition to the quantitative differences in LDL and HDL, there were significant increases in the size of the HDL, a shift to smaller LDL particles, and changes in apolipoprotein (apo) composition as evaluated by FPLC and Western blot analysis. Large apoA-I-poor and apoE-containing HDL became prevalent in hypercholesterolemic hamsters after CETP inhibition. In addition, the

size of the CETP-containing HDL particles increased with inhibition of transfer

activity. While these effects were apparent in normocholesterolemic animals, the changes in apolipoprotein distribution and HDL subspecies as detected on native gels were more significant in the hypercholesterolemic animals. The changes in the HDL profile and apolipoprotein distribution after CETP inhibition in hamsters were similar to those reported in CETP-deficient Japanese subjects, suggesting the utility of the hypercholesterolemic hamster as an in vivo model for the understanding of

L2 ANSWER 5 OF 5 MEDLINE
ACCESSION NUMBER: 89292152 MEDLINE
DOCUMENT NUMBER: 89292152
TITLE: Monoclonal antibody inhibition of cholesteryl ester transfer protein activity in the rabbit. Effects on lipoprotein composition and high density lipoprotein cholesteryl ester metabolism.
AUTHOR: Whitlock M E; Swenson T L; Ramakrishnan R;
Leonard M T; Marcel Y L; Milne R W; Tall A R
CORPORATE SOURCE: Department of Medicine, Columbia University College of Physicians & Surgeons, New York 10032.
CONTRACT NUMBER: HL-21006 (NHLBI)
HL-22682 (NHLBI)
T-07343
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1989 Jul) 84 (1)
129-37.
Journal code: HS7. ISSN: 0021-9738.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 198910
AB Cholesteryl ester transfer protein (CETP) promotes in vitro transfer of cholesteryl ester (CE) and triglyceride (TG) between lipoproteins. We studied the function of CETP in vivo in rabbit lipoprotein metabolism using a neutralizing monoclonal antibody (MAb, TP1) to CETP. Rabbits were injected with TP1 ($n = 8$), or irrelevant MAb or saline (control, $n = 8$), resulting in an initial 71% inhibition of CETP, which fell to 45% after 48 h. HDL CE rose in the inhibited animals, reaching levels that doubled initial and control values at 48 h (P less than 0.001). HDL TG fell reciprocally, but HDL protein did not change, suggesting a CE for TG exchange. VLDL CE/TG decreased. Rabbits were also given [³H]cholesteryl ether HDL (a CE analogue). CETP inhibition delayed the initial clearance of radioactivity from HDL (control 6.8 vs. TP1 4.1 pools/d) and plasma (7.8 vs. 5.2 pools/d). We conclude that CETP plays a quantitatively important role in HDL CE catabolism in the rabbit, promoting the exchange of TG for CE and the clearance of CE from plasma.

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 198807

AB A cholesteryl ester transfer protein (CETP) of apparent Mr 74,000 has recently been purified from human plasma. Three monoclonal neutralizing antibodies to the CETP were obtained by immunizing mice with purified CETP. The antibodies, each recognizing a similar epitope on CETP, caused parallel and complete immunotitration of plasma cholesteryl ester and triglyceride transfer activities but only partial inhibition of phospholipid transfer activity. Monoclonal immunoaffinity chromatography of plasma or its fractions showed complete removal of cholesteryl ester and triglyceride transfer activities but incomplete removal of phospholipid transfer activity. Sodium dodecyl sulfate gel electrophoresis

and immunoblotting of the immunoaffinity-retained fractions showed that only the Mr 74,000 protein was immunoreactive. The results suggest that the previously characterized CETP accounts for all of the cholesteryl ester and triglyceride transfer activity in human plasma but only part of

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$0.00 Estimated cost File410  
$0.03 TELNET  
$0.03 Estimated cost this search  
$0.03 Estimated total session cost 0.233 DialUnits
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File 340: CLAIMS(R) /US Patent 1950-03/Jul 22
(c) 2003 IFI/CLAIMS(R)

*File 340: The Claims U.S. Patent databases have been reloaded.
HELP NEWS340 & HELP ALERTS340 for search, display & Alert info.

Set	Items	Description
? s thyroglobulin	S1	140 THYROGLOBULIN
? s carrier	S2	196577 CARRIER
? s s1 and s2	140	S1
	196577	S2
	S3	81 S1 AND S2
? s s3 and py<=1996	81	S3
	2818513	PY<=1996
? s s4 and py<=1995	S4	52 S3 AND PY<=1996
	52	S4
	2689732	PY<=1995
? rd	S5	47 S4 AND PY<=1995
>>>Duplicate detection is not supported for File 340.		
>>>All specified files are unsupported, command ignored.		
? s vaccine	S6	4720 VACCINE
? s s5 and s6	47	S5
	4720	S6
	S7	4 S5 AND S6
? t s7/3,k,ab/1-4		

7/3,K,AB/1
DIALOG(R) File 340: CLAIMS(R) /US Patent
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Dialog Acc No: 2080710 IFI Acc No: 9020674
Document Type: C
HTLV-III (LAV) ENVELOPE PEPTIDES; USED FOR DETECTING AIDS ANTIBODIES
Inventors: Heimer Edgar P (US); Reddy Premkumar E (US)
Assignee: Hoffmann-La Roche Inc
Assignee Code: 39424
Publication (No,Date), Applic (No,Date):
US 4957737 19900918 US 89396195 19890821
Publication Kind: A
Calculated Expiration: 20070918
(Cited in 011 later patents) Document Type: EXPIRED
Continuation Pub(No),Applic(No,Date): ABANDONED US 86866817
19860527; ABANDONED US 88160847 19880201
Priority Applic(No,Date): US 89396195 19890821; US 86866817 19860527;

US 88160847 19880201

Abstract: Synthetic peptides containing the epitopic sequence HTLV env (578-608) are useful as reagents in immunoassays for detection of AIDS antibodies, as immunogens for eliciting polyclonal or monoclonal antibodies against AIDS virus env protein and as components in an AIDS vaccine.

Publication (No,Date), Applic (No,Date):
...19900918

Abstract: ... polyclonal or monoclonal antibodies against AIDS virus env protein and as components in an AIDS vaccine.

Non-exemplary Claims: ...where W is Cys or Z is Cys-NH₂, covalently bonded to an immunogenically compatible **carrier** material...

...4. The composition of claim 3, wherein said immunogenic **carrier** material is **thyroglobulin**.

7/3,K,AB/2
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2003 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 1696797 IFI Acc No: 8614604

Document Type: C

IMMUNOLOGICAL PREVENTION OF BOAR ODOR IN UNCASTRATED MALE PIGS

Inventors: BROOKS ROGER I (US); GRAY J IAN (US); HOGBERG MAYNARD G (US); PEARSON ALBERT M (US); PESTKA JAMES J (US)

Assignee: RESEARCH CORP

Assignee Code: 70917

Publication (No,Date), Applic (No,Date):

US 4610877 19860909 US 84662662 19841019

Publication Kind: A

Calculated Expiration: 20041019

(Cited in 007 later patents) Document Type: EXPIRED

Priority Applic(No,Date): US 84662662 19841019

Abstract: The present invention relates to novel immunogens which can be employed in a method for eliminating the offensive odor associated with the preparation of meats derived from uncastrated male pigs. "Boar taint," as the characteristic odor has been termed, can be eliminated, or at least substantially reduced by the administration of novel immunogen compositions which are chemical conjugates formed of certain C19 Delta 16-steroids and their mixtures with a **carrier** protein. The immunogens can be administered in conventional forms including a **vaccine**.

Publication (No,Date), Applic (No,Date):
...19860909

Abstract: ...are chemical conjugates formed of certain C19 Delta 16-steroids and their mixtures with a **carrier** protein. The immunogens can be administered in conventional forms including a **vaccine**.

Exemplary Claim: ...FOR THE ELIMINATION OF BOAR TAINT COMPRISING A C19 DELTA 16-STEROID CONJUGATE AND A **CARRIER** PROTEIN, WHEREIN THE C19 DELTA 16-STEROID IS 5,16-ANDROSTADIEN-3 BETA -OL, 4,16-ANDROSTADIEN-3-ONE AND MIXTURES THEREOF.
7. A **VACCINE** CONTAINING THE COMPOSITION OF CLAIM 2 AND A PHARMACEUTICALLY ACCEPTABLE **CARRIER**.

Non-exemplary Claims: ...claim 1, wherein at least one of said C19 Delta 16-steroid conjugates and a **carrier** protein is mixed with 5 Alpha -androst-16-en-3-one, 5 Alpha -androst-16...

...3. An immunogenic composition of claim 1, wherein said **carrier**

protein is bovine serum albumin or bovine **thyroglobulin**.

...
...6. A vaccine containing the composition of claim 1 and a pharmaceutically acceptable **carrier**.

...
...8. A vaccine of claim 6, wherein said pharmaceutically acceptable **carrier** is a water-in-oil emulsion containing sodium chloride and Freund's Incomplete Adjuvant...

...9. A vaccine of claim 7, wherein said pharmaceutically acceptable **carrier** is a water-in-oil emulsion containing sodium chloride and Freund's Incomplete Adjuvant...

...10. A vaccine of claim 8, wherein said C19 Delta 16-steroid conjugate or mixtures thereof are present...

...11. A vaccine of claim 9, wherein said C19 Delta 16-steroid conjugate or mixtures thereof are present...

...the administration of an immunogenic composition containing a C19 Delta 16-steroid conjugate to a **carrier** protein, wherein the C19 Delta 16-steroid is 5,16-androstadien-3 Beta -ol, 4...

...claim 12, wherein at least one of said C19 Delta 16-steroid conjugate and a **carrier** protein is mixed with 5 Alpha -androst-16-en-3-one, 5 Alpha -androst-16...

...14. A method of claim 12, wherein said protein **carrier** is bovine serum albumin or bovine **thyroglobulin**.

7/3,K,AB/3

DIALOG(R) File 340:CLAIMS(R)/US Patent
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Dialog Acc No: 1684097 IFI Acc No: 8610729

Document Type: C

SYNTHETIC HEPATITIS B VIRUS VACCINE INCLUDING BOTH T CELL AND B CELL DETERMINANTS; MIXTURES OF POLYPEPTIDES

Inventors: CHISARI FRANK V (US); MILICH DAVID R (US)

Assignee: SCRIPPS CLINIC & RESEARCH FOUNDATION

Assignee Code: 03325 Document Type: REASSIGNED

Publication (No,Date), Applic (No,Date):

US 4599231 19860708 US 84587983 19840309

Publication Kind: A

Calculated Expiration: 20040309

(Cited in 034 later patents) Document Type: EXPIRED

Priority Applic(No,Date): US 84587983 19840309

Abstract: Chemically synthesized polypeptides include amino acid residue sequences that substantially correspond to the amino acid residue sequences of T Cell and B cell determinant portions of a natural, pathogen-related protein, in particular, a hepatitis B virus surface antigen (HBsAG). When administered to a host alone, as polymers or as **carrier**-bound conjugates, the polypeptides induce the proliferation of thymus-derived cells in hosts primed against hepatitis B virus.

SYNTHETIC HEPATITIS B VIRUS VACCINE INCLUDING BOTH T CELL AND B CELL DETERMINANTS...

Publication (No,Date), Applic (No,Date):

...19860708

Abstract: ...B virus surface antigen (HBsAG). When administered to a host alone, as polymers or as carrier-bound conjugates, the polypeptides induce the proliferation of thymus-derived cells in hosts primed against...

Exemplary Claim: 1. A VACCINE AGAINST INFECTION BY HEPATITIS B VIRUS COMPRISING: (A) AN EFFECTIVE AMOUNT OF AT LEAST ONE...

...METTHRTHRALAGLNGLYTHR SERMETTYR PROSER CYS;
ILEPROGLYSERTHRTHR SERTHRG LYPRO CYS LYSTHRCYS
THRTHR PROALAGLNGLYASN SERMETPHE PROSER CYS;
THRTHR PROALAGLNGLYASN SERMETPHE PROSER CYS; AND
CYS PROLEUILEPROGLYSERTHRTHR SERTHRG LYPRO
CYS LYSTHRCYS THR PROALAGLNGLYASN SERMET PHE PROSER CYS; AND (C) A
PHYSIOLOGICALLY TOLERABLE DILUENT, SAID VACCINE WHEN INTRODUCED
INTO A HOST, BEING CAPABLE OF INDUCING THE PRODUCTION OF ANTIBODIES AND
THE...

...DERIVED CELLS IN THE HOST, SAID ANTIBODIES IMMUNOREACTING WITH SAID
HEPATITIS B VIRUS, AND SAID VACCINE PROTECTING THE HOST FROM
HEPATITIS B VIRAL INFECTION.

Non-exemplary Claims: 2. The vaccine according to claim 1 wherein
said physiologically tolerable diluent is a member of the group...

...3. The vaccine according to claim 1 wherein said synthetic
polypeptides are bound to a carrier.

...

...4. The vaccine according to claim 1 wherein said carrier is
selected from the group consisting of keyhole limpet hemocyanin, keyhole
limpet hemocyanin in incomplete...

...s adjuvant, alum, keyhole limpet hemocyanin-alum absorbed, keyhole
limpet hemocyanin-alum absorbed-pertussis, edestin, thyroglobulin,
tetanus toxoid, tetanus toxoid in incomplete Freund's adjuvant, cholera
toxoid and cholera toxoid in...

...5. A vaccine against infection by hepatitis B virus comprising an
effective amount of a synthetic polypeptide having...

...positions 110 to 137 from the amino-terminus thereof, and a
physiologically tolerable diluent, said vaccine when introduced
into a host, being capable of inducing the production of antibodies and
the...

...derived cells in the host, said antibodies immunoreacting with said
hepatitis B virus and said vaccine protecting the host from
hepatitis B viral infection...

...6. The vaccine according to claim 5 wherein the synthetic
polypeptide includes the sequences of amino acid residues...

...7. A vaccine against infection by hepatitis B virus comprising an
effective amount of a synthetic polypeptide having...

...positions 110 to 137 from the amino-terminus thereof, and a
physiologically tolerable diluent, said vaccine when introduced
into a host, being capable of inducing the production of antibodies and
the...

...derived cells in the host, said antibodies immunoreacting with said
hepatitis B virus and said vaccine protecting the host from
hepatitis B viral infection...

...8. The vaccine according to claim 7 wherein the synthetic

polypeptide includes the sequences of amino acid residues...

...9. A vaccine against infection by hepatitis B virus comprising an effective amount of a synthetic polypeptide having...

...positions 95 to 137 from the amino-terminus thereof, and a physiologically tolerable diluent, said vaccine when introduced into a host, being capable of inducing the production of antibodies and the...

...derived cells in the host, said antibodies immunoreacting with said hepatitis B virus and said vaccine protecting the host from hepatitis B viral infection¹⁰. The vaccine according to claim 9 wherein the synthetic polypeptide includes the sequence of amino acid residues...

...11. A vaccine against infection by hepatitis B virus comprising an effective amount of a synthetic multimer in...

...intramolecular cystine disulfide bond formed from at least two of the Cys residues present, said vaccine when introduced into a host, being capable of inducing the production of antibodies and the...

...derived cells in the host, said antibodies immunoreacting with said hepatitis B virus, and said vaccine protecting the host from hepatitis B viral infection...

...12. The vaccine according to claim 11 wherein said physiologically tolerable diluent is a member of the group...

...13. The vaccine according to claim 11 wherein said synthetic multimer is bound to a carrier.

...

...14. The vaccine according to claim 11 wherein said carrier is selected from the group consisting of keyhole limpet hemocyanin, keyhole limpet hemocyanin in incomplete...

...s adjuvant, alum, keyhole limpet hemocyanin-alum absorbed, keyhole limpet hemocyanin-alum absorbed-pertussis, edestin, thyroglobulin, tetanus toxoid, tetanus toxoid in incomplete Freund's adjuvant, cholera toxoid and cholera toxoid in...

...15. The vaccine according to claim 11 wherein the intramolecular cystine disulfide bond of said synthetic multimer is...

...16. The vaccine according to claim 11 wherein the polypeptide repeating units of said synthetic multimer are bonded...

...17. The vaccine according to claim 16 wherein said synthetic multimer contains about two to about three of...

...18. The vaccine according to claim 11 wherein the intramolecular cystine disulfide bond of said synthetic multimer is...

...19. The vaccine according to claim 18 wherein the polypeptide repeating units of said synthetic multimer are bonded²⁰. A vaccine against infection by hepatitis B virus comprising a physiologically tolerable diluent having dispersed therein (i...

...the direction from amino-terminus to carboxy-terminus, and represented by the formula: SerLeuAsnPheLeuGlyGlyThrThrValCysLeuGlyGlnAsn; said vaccine, when introduced into a host, being capable of inducing the production of antibodies and the...

...derived cells in the host, said antibodies immunoreacting with said hepatitis B virus and said **vaccine** protecting the host from hepatitis B viral infection...

...21. A **vaccine** against infection by hepatitis B virus comprising a physiologically tolerable diluent having dispersed therein (i...
...the direction from amino-terminus to carboxy-terminus, and represented by the formula: ValCysLeuGlyGlnAsn; said **vaccine**, when introduced into a host, being capable of inducing the production of antibodies and the...

...derived cells in the host, said antibodies immunoreacting with said hepatitis B virus and said **vaccine** protecting the host from hepatitis B viral infection...

...22. A **vaccine** against infection by hepatitis B virus comprising a physiologically tolerable diluent having dispersed therein an...

...acid residue in parentheses is an alternative to the immediately preceding amino acid residue, said **vaccine**, when introduced into a host, being capable of inducing the production of antibodies and the...

...derived cells in the host, said antibodies immunoreacting with said hepatitis B virus and said **vaccine** protecting the host from hepatitis B viral infection.

7/3,K,AB/4

DIALOG(R) File 340:CLAIMS(R)/US Patent
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Dialog Acc No: 1684096 IFI Acc No: 8610728

Document Type: C

SYNTHETIC HEPATITIS B VIRUS VACCINE INCLUDING BOTH T CELL AND B CELL DETERMINANTS; POLYPEPTIDE ANTIGENS

Inventors: CHISARI FRANK V (US); MILICH DAVID R (US)

Assignee: SCRIPPS CLINIC & RESEARCH FOUNDATION

Assignee Code: 03325 Document Type: REASSIGNED

Publication (No,Date), Applic (No,Date):

US 4599230 19860708 US 84588122 19840309

Publication Kind: A

Calculated Expiration: 20040309

(Cited in 035 later patents) Document Type: EXPIRED Document Type:

CERTIFICATE OF CORRECTION Certificate of Correction Date: 19880614

Priority Applic(No,Date): US 84588122 19840309

Abstract: Chemically synthesized polypeptides include amino acid residue sequences that substantially correspond to the amino acid residue sequences of T cell and B cell determinant portions of a natural, pathogen-related protein, in particular, a hepatitis B virus surface antigen (HBsAg). When administered to a host alone, as polymers or as **carrier-bound** conjugates, the polypeptides induce the proliferation of thymus-derived cells in hosts primed against hepatitis B virus.

SYNTHETIC HEPATITIS B VIRUS VACCINE INCLUDING BOTH T CELL AND B CELL DETERMINANTS...

Publication (No,Date), Applic (No,Date):

...19860708

Abstract: ...B virus surface antigen (HBsAg). When administered to a host alone, as polymers or as **carrier-bound** conjugates, the polypeptides induce the proliferation of thymus-derived cells in hosts primed against...

Exemplary Claim: 1. A VACCINE AGAINST INFECTION BY HEPATITIS B VIRUS
COMPRISING: (A) AN EFFECTIVE AMOUNT OF A SYNTHETIC POLYPEPTIDE...

...METTHRTHRALAGLNGLYTHR SERMETTYRPROSER CYS;
ILEPROGLYSERTHRTHR SERTHRG LYPRO CYSLYSTHRCYS
THRTHR PROALAGLNGLYASN SERMETPHEPROSER CYS;
THRTHR PROALAGLNGLYASN SERMETPHEPROSER CYS; AND
CYS PROLEUILEPROGLYSERTHRTHR SERTHRG LYPRO
CYSLYSTHRCYS THRPROALAGLNGLYASN SERMETPHEPROSER CYS; AND (C) A
PHYSIOLOGICALLY TOLERABLE DILUENT, SAID VACCINE WHEN INTRODUCED
INTO A HOST, BEING CAPABLE OF INDUCING THE PRODUCTION OF ANTIBODIES AND
THE...

...DERIVED CELLS IN THE HOST, SAID ANTIBODIES IMMUNOREACTING WITH SAID
HEPATITIS B VIRUS, AND SAID VACCINE PROTECTING THE HOST FROM
HEPATITIS B VIRAL INFECTION.

Non-exemplary Claims: 2. The vaccine according to claim 1 wherein
said physiologically tolerable diluent is a member of the group...

...3. The vaccine according to claim 1 wherein said synthetic
polypeptides are bound to a carrier.

...

...4. The vaccine according to claim 1 wherein said carrier is
selected from the group consisting of keyhole limpet hemocyanin, keyhole
limpet hemocyanin in incomplete...

...s adjuvant, alum, keyhole limpet hemocyanin-alum absorbed, keyhole
limpet hemocyanin-alum absorbed-pertussis, edestin, thyroglobulin,
tetanus toxoid, tetanus toxoid in incomplete Freund's adjuvant, cholera
toxoid and cholera toxoid in...

...5. A vaccine against infection by hepatitis B virus comprising an
effective amount of a synthetic polypeptide having...

...positions 110 to 137 from the amino-terminus thereof, and a
physiologically tolerable diluent, said vaccine when introduced
into a host, being capable of inducing the production of antibodies and
the...

...derived cells in the host, said antibodies immunoreacting with said
hepatitis B virus and said vaccine protecting the host from
hepatitis B viral infection...

...6. The vaccine according to claim 5 wherein the synthetic
polypeptide includes the sequences of amino acid residues...

...7. A vaccine against infection by hepatitis B virus comprising an
effective amount of a synthetic polypeptide having...

...positions 110 to 154 from the amino-terminus thereof, and a
physiologically tolerable diluent, said vaccine when introduced
into a host, being capable of inducing the production of antibodies and
the...

...derived cells in the host, said antibodies immunoreacting with said
hepatitis B virus and said vaccine protecting the host from
hepatitis B viral infection...

...8. The vaccine according to claim 7 wherein the synthetic
polypeptide includes the sequence of amino acid residues...

...9. A vaccine against infection by hepatitis B virus comprising an
effective amount of a synthetic multimer in...

...intramolecular cystine disulfide bond formed from at least two of the Cys residues present, said **vaccine** when introduced into a host, being capable of inducing the production of antibodies and the in the host, said antibodies immunoreacting with said hepatitis B virus, and said **vaccine** protecting the host from hepatitis B viral infection
...

...10. The **vaccine** according to claim 9 wherein said physiologically tolerable diluent is a member of the group...

...11. The **vaccine** according to claim 9 wherein said synthetic multimer is bound to a **carrier**.
...

...12. The **vaccine** according to claim 9 wherein said **carrier** is selected from the group consisting of keyhole limpet hemocyanin, keyhole limpet hemocyanin in incomplete...

...s adjuvant, alum, keyhole limpet hemocyanin-alum absorbed, keyhole limpet hemocyanin-alum absorbed-pertussis, edestin, **thyroglobulin**, tetanus toxoid, tetanus toxoid in incomplete Freund's adjuvant, cholera toxoid and cholera toxoid in...

...13. The **vaccine** according to claim 9 wherein the intramolecular cystine disulfide bond of said synthetic multimer is...

...14. The **vaccine** according to claim 9 wherein the polypeptide repeating units of said synthetic multimer are bonded...

...15. The **vaccine** according to claim 14 wherein said synthetic multimer contains about two to about three of...

...16. The **vaccine** according to claim 9 wherein the intramolecular cystine disulfide bond of said synthetic multimer is...

...17. The **vaccine** according to claim 16 wherein the polypeptide repeating units of said synthetic multimer are bonded...

...18. A **vaccine** against infection by hepatitis B virus comprising a physiologically tolerable diluent having dispersed therein (i...
...direction from amino-terminus to carboxy-terminus, and represented by the formula: ThrLysProSerAspGlyAsnCysThr CysIleProIleProSer; said **vaccine**, when introduced into a host, being capable of inducing the production of antibodies and the...
...derived cells in the host, said antibodies immunoreacting with said hepatitis B virus and said **vaccine** protecting the host from hepatitis B viral infection...

...19. A **vaccine** against infection by hepatitis B virus comprising a physiologically tolerable diluent having dispersed therein an to the immediately preceding amino acid residue, said **vaccine**, when introduced into a host, being capable of inducing the production of antibodies and the...
...derived cells in the host, said antibodies immunoreacting with said hepatitis B virus and said **vaccine** protecting the host from hepatitis B viral infection.

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STEM:OS - DIALOG OneSearch
File 155: MEDLINE(R) 1966-2003/Jul W4
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*File 155: Medline has been reloaded and accession numbers have changed. Please see HELP NEWS 155.
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File 34:SciSearch(R) Cited Ref Sci 1990-2003/Jul W3
(c) 2003 Inst for Sci Info
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
(c) 1998 Inst for Sci Info
File 340:CLAIMS(R)/US Patent 1950-03/Jul 22
(c) 2003 IFI/CLAIMS(R)
*File 340: The Claims U.S. Patent databases have been reloaded. HELP NEWS340 & HELP ALERTS340 for search, display & Alert info.

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90 OLIGOLYSINE
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2/3,K,AB/1 (Item 1 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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08223941 94289895 PMID: 8019057
Immunization and affinity purification of antibodies using resin-immobilized lysine-branched synthetic peptides.
Butz S; Rawer S; Rapp W; Birsner U
Max-Planck-Institut fur Immunobiologie, Germany.
Peptide research (UNITED STATES) Jan-Feb 1994, 7 (1) p20-3, ISSN 1040-5704 Journal Code: 8913494

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A new method has been developed to raise antibodies against synthetic peptides. A multiple antigenic peptide system (MAP) containing a branched oligolysine was synthesized on a beaded polystyrene polyoxyethylene graft copolymer resin, which acts as a synthetic hapten carrier for use in immunization. The peptides, already attached to the carrier, can be used directly after final deprotection without any further purification steps. The utility of this peptide-carrier conjugate is highlighted by its additional application for affinity purification of antibodies generated.

... developed to raise antibodies against synthetic peptides. A multiple antigenic peptide system (MAP) containing a branched oligolysine was synthesized on a beaded polystyrene polyoxyethylene graft copolymer resin, which acts as a synthetic...

2/3,K,AB/2 (Item 1 from file: 340)
DIALOG(R) File 340: CLAIMS(R)/US Patent

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Dialog Acc No: 10282404 IFI Acc No: 2003-0026808 IFI Acc No: 2003-0006652

Document Type: C

AN IMMUNOLOGICAL PROCESS FOR INCREASING THE HDL CHOLESTROL CONCENTRATION

Inventors: GAMSON EDWARD P (US); GLENN KEVIN (US); KRUL ELAINE (US);
NEEDLEMAN PHILIP (US)

Assignee: Unassigned Or Assigned To Individual

Assignee Code: 68000

Publication (No,Date), Applic (No,Date):

US 20030026808 20030206 US 99387340 19990831

Publication Kind: A1

Continuation Pub(No),Applic(No,Date): PENDING US 97788882
19970121

Priority Applic(No,Date): US 99387340 19990831; US 97788882 19970121

Abstract: A process for increasing the concentration of HDL cholesterol in the blood of a mammal whose blood contains cholesterol ester transfer protein (CETP) is contemplated. That process comprises the steps of: (a) immunizing the mammal with an inoculum containing a CETP immunogen that is an immunogenic polypeptide having a CETP amino acid residue sequence that is covalently bonded to an exogenous antigenic carrier polypeptide and is dissolved or dispersed in a vehicle; and (b) maintaining the immunized mammal for a time period sufficient for said immunogenic polypeptide to induce the production of antibodies that bind to CETP and lessen the transfer of cholesteryl esters from HDL. Immunogens, inocula and DNA segments useful for carrying out the invention are also disclosed.

Exemplary Claim: ...consisting of hepatitis B core protein, tetanus toxoid, tuberculin purified protein derivative, diphtheria toxoid and **branched oligolysine**, said immunogenic polypeptide having a CETP amino acid residue sequence; and (b) maintaining said immunized...

?

SYSTEM:OS - DIALOG OneSearch
File 155:MEDLINE(R) 1966-1999/Dec W4
(c) format only 1999 Dialog Corporation
File 55:BIOSIS Previews(R) 1993-1999/Nov W3
(c) 1999 BIOSIS
File 34:SCISEARCH(R) CITED REF SCI 1990-1999/DEC W4
(c) 1999 INST FOR SCI INFO
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
(c) 1998 Inst for Sci Info
File 340:CLAIMS(R)/US PATENT 1950-99/DEC 21
(c) 1999 IFI/CLAIMS(R)

*File 340: *** Annual reload now online. *** See HELP NEWS 340
for more information.

Set Items Description

--- -----

? s cholesteryl(w)ester(w)transfer or cetp

14970 CHOLESTERYL
253795 ESTER
647005 TRANSFER
3588 CHOLESTERYL(W)ESTER(W)TRANSFER
1584 CETP

S1 3824 CHOLESTERYL(W)ESTER(W)TRANSFER OR CETP

? s tetanus or tuberculin or diphtheria or oligolysine

23975 TETANUS
14912 TUBERCULIN
14344 DIPHTHERIA
40 OLIGOLYSINE

S2 47356 TETANUS OR TUBERCULIN OR DIPHTHERIA OR OLIGOLYSINE

? s s1 and s2

3824 S1
47356 S2
S3 0 S1 AND S2

Ab to CETP: (cannot make too negative, b/c. it is not
know whether such immunization
blocks by 100% or more. According to
Gray's, inhibition of Ab
against CETP only
in mice)

6/3, K, AB/1 (Item 1 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

(c) format only 1999 Dialog Corporation. All rts. reserv.

08938557 97070859

Mouse monoclonal antipeptide antibodies specific for cholesteryl ester transfer protein (CETP).

Thomas AP; Smith AM; Cumming RI; Jones C; Thomas RC; Pleasants KT; Barakat H

Department of Microbiology and Immunology, East Carolina University School of Medicine, Greenville, North Carolina 27858-4354, USA.

Hybridoma (UNITED STATES) Oct 1996, 15 (5) p359-64, ISSN 0272-457X

Journal Code: GFS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A synthetic peptide whose amino acid sequence corresponds to residues 131-142 of human cholesteryl ester transfer protein (CETP) was used as an immunogen to generate a panel of monoclonal antibodies (MAbs) specific for the intact CETP molecule. Spleen cells from BALB/c mice immunized with the peptide conjugated with keyhole limpet hemocyanin (KLH) were fused with SP2/0 myeloma cells. Two MAbs that bound fixed peptide in an enzyme-linked immunoabsorbent assay (ELISA) were partially characterized regarding their specificity and biological activity. ATM192 of the IgG1 subclass and J16-14 of the IgG3 subclass were used in a Western blot assay as well as in the ELISA. We have also shown through the use of immunoprecipitation that ATM192 can remove CETP enzyme activity from human serum without destroying the enzyme's activity. We have also shown that the antibodies can bind CETP from rabbits. The specificity studies and the lack of inhibition of enzymatic activity suggest that the MAbs bind a structural area of the CETP molecule not a part of the active binding site of the enzyme. We conclude that these antibodies can be valuable as tools for studying CETP levels in human serum as well as in tissue homogenates from rabbits and humans.

Mouse monoclonal antipeptide antibodies specific for cholesteryl ester transfer protein (CETP).

A synthetic peptide whose amino acid sequence corresponds to residues 131-142 of human cholesteryl ester transfer protein (CETP) was used as an immunogen to generate a panel of monoclonal antibodies (MAbs) specific for the intact CETP molecule. Spleen cells from BALB/c mice immunized with the peptide conjugated with keyhole limpet hemocyanin (KLH) were fused with SP2/0 myeloma...

... the ELISA. We have also shown through the use of immunoprecipitation that ATM192 can remove CETP enzyme activity from human serum without destroying the enzyme's activity. We have also shown that the antibodies can bind CETP from rabbits. The specificity studies and the lack of inhibition of enzymatic activity suggest that the MAbs bind a structural area of the CETP molecule not a part of the active binding site of the enzyme. We conclude that these antibodies can be valuable as tools for studying CETP levels in human serum as well as in tissue homogenates from rabbits and humans.

Descriptors: Antibodies, Monoclonal--Chemistry--CH; *Antibody Specificity; *Carrier Proteins--Immunology--IM; *Cholesterol Esters--Immunology--IM; *Peptides--Immunology--IM

Chemical Name: cholesterol ester transfer proteins; (Antibodies, Monoclonal; (Carrier Proteins; (Cholesterol Esters; (Peptides

05499476 88186779

Monoclonal antibodies to the Mr 74,000 cholesteryl ester transfer protein neutralize all of the cholesteryl ester and triglyceride transfer activities in human plasma.

Hesler CB; Tall AR; Swenson TL; Weech PK; Marcel YL; Milne RW

Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York 10032.

J Biol Chem (UNITED STATES) Apr 15 1988, 263 (11) p5020-3, ISSN 0021-9258 Journal Code: HIV

Contract/Grant No.: HL22682, HL, NHLBI; T-07343

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A cholesteryl ester transfer protein (CETP) of apparent Mr 74,000 has recently been purified from human plasma. Three monoclonal neutralizing antibodies to the CETP were obtained by immunizing mice with purified CETP. The antibodies, each recognizing a similar epitope on CETP, caused parallel and complete immunotitration of plasma cholesteryl ester and triglyceride transfer activities but only partial inhibition of phospholipid transfer activity. Monoclonal immunoaffinity chromatography of plasma or its fractions showed complete removal of cholesteryl ester and triglyceride transfer activities but incomplete removal of phospholipid transfer activity. Sodium dodecyl sulfate gel electrophoresis and immunoblotting of the immunoaffinity-retained fractions showed that only the Mr 74,000 protein was immunoreactive. The results suggest that the previously characterized CETP accounts for all of the cholesteryl ester and triglyceride transfer activity in human plasma but only part of the phospholipid transfer activity.

Monoclonal antibodies to the Mr 74,000 cholesteryl ester transfer protein neutralize all of the cholesteryl ester and triglyceride transfer activities in human plasma.

A cholesteryl ester transfer protein (CETP) of apparent Mr 74,000 has recently been purified from human plasma. Three monoclonal neutralizing antibodies to the CETP were obtained by immunizing mice with purified CETP. The antibodies, each recognizing a similar epitope on CETP, caused parallel and complete immunotitration of plasma cholesteryl ester and triglyceride transfer activities but only...

... only the Mr 74,000 protein was immunoreactive. The results suggest that the previously characterized CETP accounts for all of the cholesteryl ester and triglyceride transfer activity in human plasma but...

Descriptors: Antibodies, Monoclonal; *Carrier Proteins--Immunology --IM; *Cholesterol Esters--Blood--BL; *Triglycerides--Blood--BL; Carrier Proteins--Blood--BL; Chromatography, Affinity; Cross Reactions; Immunosorbent Techniques; Molecular Weight; Rabbits Chemical Name: cholesterol ester transfer proteins; (Antibodies, Monoclonal; (Carrier Proteins; (Cholesterol Esters; (Triglycerides

05015522 87137455

Purification and characterization of a human plasma cholesteryl ester transfer protein.

Hesler CB; Swenson TL; Tall AR

J Biol Chem (UNITED STATES) Feb 15 1987, 262 (5) p2275-82, ISSN

Looked at full tape
did no say whether CETP was linked to a carrier or CETP by itself was infected

0021-9258 Journal Code: HIV
Contract/Grant No.: HL 22682, HL, NHLBI; T-07343
Languages: ENGLISH
Document type: JOURNAL ARTICLE

The **cholesteryl ester transfer protein (CETP)** binds to plasma lipoproteins and promotes transfer of cholesteryl esters between the lipoproteins. **CETP** has been purified 55,000-fold, with a 27% recovery of activity, from the d greater than 1.21 g/ml fraction of human plasma. In the final purification step, partially purified **CETP** is incubated with a synthetic lipid emulsion consisting of phosphatidylcholine, triglyceride, and fatty acid, and the bound activity, which elutes in the void volume, is separated from nonbound proteins by gel filtration on Sepharose 4B. Sodium dodecyl sulfate-gel analysis of fractions containing bound activity shows the presence of a single protein with an apparent Mr of 74,000. Inclusion of fatty acid in this emulsion was required to prevent the binding of a contaminant protein. However, incubation of **CEPT** with fatty acid emulsions containing lipid peroxides resulted in substantial inactivation and covalent degradation of the 74-kDa protein. This could be prevented by the inclusion of antioxidants during preparation of the emulsion. Solvent extraction of emulsion-bound **CEPT** gave a delipidated, active preparation. Purified IgG from a rabbit immunized with the 74-kDa protein completely removed activity from partially purified fractions. Amino acid analysis of the purified protein showed it to contain an unusually high content (45%) of nonpolar residues; the calculated hydrophobicity was greater than that of any other plasma apolipoprotein. These results show human **CETP** to be a unique plasma apolipoprotein with an apparent Mr of 74,000 which is hydrophobic, self-associating, and susceptible to covalent degradation by lipid peroxides.

Purification and characterization of a human plasma **cholesteryl ester transfer protein**.

The **cholesteryl ester transfer protein (CETP)** binds to plasma lipoproteins and promotes transfer of cholesteryl esters between the lipoproteins. **CETP** has been purified 55,000-fold, with a 27% recovery of activity, from the d...

... 1.21 g/ml fraction of human plasma. In the final purification step, partially purified **CETP** is incubated with a synthetic lipid emulsion consisting of phosphatidylcholine, triglyceride, and fatty acid, and...

... extraction of emulsion-bound **CEPT** gave a delipidated, active preparation. Purified IgG from a rabbit immunized with the 74-kDa protein completely removed activity from partially purified fractions. Amino acid analysis...

... calculated hydrophobicity was greater than that of any other plasma apolipoprotein. These results show human **CETP** to be a unique plasma apolipoprotein with an apparent Mr of 74,000 which is...

Descriptors: **Carrier Proteins--Isolation and Purification--IP**

Chemical Name: cholesterol ester transfer proteins; (Amino Acids; (Apolipoproteins; (**Carrier Proteins**

```
? s cetp or cholesteryl(w)ester(w)transfer
    1582  CETP
    14954 CHOLESTERYL
    253719 ESTER
    646784 TRANSFER
    3586 CHOLESTERYL(W)ESTER(W)TRANSFER
S1     3822 CETP OR CHOLESTERYL(W)ESTER(W)TRANSFER
? s carrier
    S2   305303 CARRIER
? s s1 and s2
    3822  S1
    305303 S2
    S3   647  S1 AND S2
? s immuniz?
    S4   140623 IMMUNIZ?
? s s3 and s4
    647  S3
    140623 S4
    S5     3  S3 AND S4
? rd
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>>>Records from unsupported files will be retained in the RD set.
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(Apolipoproteins; (Carrier Proteins
? ds

Set	Items	Description
S1	3822	CETP OR CHOLESTERYL (W) ESTER (W) TRANSFER
S2	305303	CARRIER
S3	647	S1 AND S2
S4	140623	IMMUNIZ?
S5	3	S3 AND S4
S6	3	RD (unique items)

? s conjugat? or link?

180964	CONJUGAT?
774522	LINK?
S7 937912	CONJUGAT? OR LINK?

? s s1 and s7

3822	S1
937912	S7
S8 282	S1 AND S7

? s immnuniz? or vaccin?

3	IMMNUNIZ?
220734	VACCIN?
S9 220737	IMMNUNIZ? OR VACCIN?

? s s8 and s9

282	S8
220737	S9
S10 1	S8 AND S9

? t s10/3,k,ab/1

10/3,K,AB/1 (Item 1 from file: 34)
DIALOG(R) File 34:SCISEARCH(R) CITED REF SCI
(c) 1999 INST FOR SCI INFO. All rts. reserv.

02397443 Genuine Article#: KY951 Number of References: 448
Title: THE QUESTIONABLE ROLES OF THE DIET AND SERUM-CHOLESTEROL IN THE
INCIDENCE OF ISCHEMIC-HEART-DISEASE AND ITS 20TH-CENTURY CHANGES

Author(s): ROSENMAN RH

Corporate Source: 2200 PACIFIC AVE 10E/SAN FRANCISCO//CA/94115; SRI
INT, HLTH SCI PROGRAM/MENLO PK//CA/94025; UNIV CALIF SAN FRANCISCO, MT
ZION MED CTR/SAN FRANCISCO//CA/94143

Journal: HOMEOSTASIS IN HEALTH AND DISEASE, 1993, V34, N1-2, P1-44

ISSN: 0960-7560

Language: ENGLISH Document Type: REVIEW

Abstract: This review is concerned with reexamining actual findings from many studies that are relevant to the relationships between risk factors and the progression of coronary artery disease and incidence of ischemic heart disease (IHD), and particularly to ascertain whether dietary and lipid variables account for 20th century changes in IHD incidence. Various published commentaries on the studies are included.

The classical risk factors are statistically related to IHD, but in widely different historical, geographical, and socioeconomic relationships they do not support a major diet-lipid causality. Even when considered together, the risk factors account for less than half

of the IHD incidence in prospective studies, and have a limited overall capability for IHD prediction. Moreover, they are poorly related to the rate of CAD progression, and lack individual specificity of risk. Many cited findings support a belief that the risk factor concept is not well suited for community prevention of IHD, among other things, because it is based on cohorts that do not represent the general population, and on the assumption that their avoidance would necessarily prevent IHD.

The serum cholesterol (SC) level is not found to be strongly related to the diet or primarily regulated by it, and many findings discordant with widespread beliefs about a causal role of the diet and SC in IHD are cited. These data lead to a conclusion that neither diet, serum lipids, or their changes can explain wide national and regional differences of IHD rates, or the variable 20th century rises and declines of IHD mortality.

This conclusion is supported by the results of many clinical trials which fail to provide adequate evidence that lowering SC, particularly by dietary changes, is associated with a significant reduction of IHD mortality or improved longevity. It is variously stated that the preventive effects of dietary and drug treatments have been exaggerated by a tendency in trial reports, reviews, and other papers to cite and inflate supportive results, while suppressing discordant data, and many such examples are cited. This review does not find sufficient data to recommend mass population changes of the diet to prevent IHD, and supports a belief that it may be evangelical to believe that a lower SC is better for everybody, rather than using an individualized approach in appropriate subjects.

...Research Fronts: LOW-DENSITY-LIPOPROTEIN CHOLESTEROL;

HYPERCHOLESTOLEMIC MEN)

91-0163 001 (INVASIVE HAEMOPHILUS-INFLUENZAE TYPE-B DISEASE;
CONJUGATE VACCINES; RESPIRATORY SYNCYTIAL VIRUS; CHILDREN
AT RISK)

91-0513 001 (ISOLATED SYSTOLIC HYPERTENSION; ANTIHYPERTENSIVE THERAPY;
CARDIOVASCULAR...

...DISEASE RISK)

91-1450 001 (APOLIPOPROTEIN A-I; CORONARY-ARTERY DISEASE;
HIGH-DENSITY-LIPOPROTEIN PARTICLES; CHOLESTERYL ESTER
TRANSFER PROTEIN; RISK OF MYOCARDIAL-INFARCTION)

91-2100 001 (FOOD FREQUENCY QUESTIONNAIRE; NUTRIENT INTAKE; WOMEN
(DUTCH...

? s cetp or cholesteryl(w)ester(w)transfer

1582	CETP
14954	CHOLESTERYL
253719	ESTER
646784	TRANSFER
3586	CHOLESTERYL(W)ESTER(W)TRANSFER
S1	3822 CETP OR CHOLESTERYL(W)ESTER(W)TRANSFER

? s carrier

S2	305303 CARRIER
----	----------------

? s s1 and s2

3822	S1
305303	S2
S3	647 S1 AND S2

? s conjugat? or link?

180964	CONJUGAT?
774522	LINK?
S4	937912 CONJUGAT? OR LINK?

? s s3 and s4

647	S3
937912	S4
S5	50 S3 AND S4

? s amino(w)terminus or carboxy(w)terminus

996157	AMINO
76762	TERMINUS
10762	AMINO(W)TERMINUS
64653	CARBOXY
76762	TERMINUS
5267	CARBOXY(W)TERMINUS
S6	15144 AMINO(W)TERMINUS OR CARBOXY(W)TERMINUS

? s s5 and s6

50	S5
15144	S6
S7	0 S5 AND S6

? rd s5

>>>Duplicate detection is not supported for File 340.

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...examined 50 records (50)
...completed examining records
S8 49 RD S5 (unique items)

? s s8 and py<1997

Processing
Processing
Processing

49	S8
29205717	PY<1997
S9	33 S8 AND PY<1997

? t s9/3,k,ab/1-33

08938557 97070859

Mouse monoclonal antipeptide antibodies specific for **cholesteryl ester transfer protein (CETP)**.

Thomas AP; Smith AM; Cumming RI; Jones C; Thomas RC; Pleasants KT; Barakat H

Department of Microbiology and Immunology, East Carolina University School of Medicine, Greenville, North Carolina 27858-4354, USA.

Hybridoma (UNITED STATES) Oct 1996, 15 (5) p359-64, ISSN 0272-457X Journal Code: GFS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A synthetic peptide whose amino acid sequence corresponds to residues 131-142 of human **cholesteryl ester transfer protein (CETP)** was used as an immunogen to generate a panel of monoclonal antibodies (MAbs) specific for the intact **CETP** molecule. Spleen cells from BALB/c mice immunized with the peptide conjugated with keyhole limpet hemocyanin (KLH) were fused with SP2/0 myeloma cells. Two MAbs that bound fixed peptide in an enzyme-linked immunoabsorbent assay (ELISA) were partially characterized regarding their specificity and biological activity. ATM192 of the IgG1 subclass and J16-14 of the IgG3 subclass were used in a Western blot assay as well as in the ELISA. We have also shown through the use of immunoprecipitation that ATM192 can remove **CETP** enzyme activity from human serum without destroying the enzyme's activity. We have also shown that the antibodies can bind **CETP** from rabbits. The specificity studies and the lack of inhibition of enzymatic activity suggest that the MAbs bind a structural area of the **CETP** molecule not a part of the active binding site of the enzyme. We conclude that these antibodies can be valuable as tools for studying **CETP** levels in human serum as well as in tissue homogenates from rabbits and humans.

Mouse monoclonal antipeptide antibodies specific for **cholesteryl ester transfer protein (CETP)**.

Oct 1996,

A synthetic peptide whose amino acid sequence corresponds to residues 131-142 of human **cholesteryl ester transfer protein (CETP)** was used as an immunogen to generate a panel of monoclonal antibodies (MAbs) specific for the intact **CETP** molecule. Spleen cells from BALB/c mice immunized with the peptide conjugated with keyhole limpet hemocyanin (KLH) were fused with SP2/0 myeloma cells. Two MAbs that bound fixed peptide in an enzyme-linked immunoabsorbent assay (ELISA) were partially characterized regarding their specificity and biological activity. ATM192 of the...

... the ELISA. We have also shown through the use of immunoprecipitation that ATM192 can remove **CETP** enzyme activity from human serum without destroying the enzyme's activity. We have also shown that the antibodies can bind **CETP** from rabbits. The specificity studies and the lack of inhibition of enzymatic activity suggest that the MAbs bind a structural area of the **CETP** molecule not a part of the active binding site of the enzyme. We conclude that these antibodies can be valuable as tools for studying **CETP** levels in human serum as well as in tissue homogenates from rabbits and humans.

Descriptors: Antibodies, Monoclonal--Chemistry--CH; *Antibody Specificity ; *Carrier Proteins--Immunology--IM; *Cholesterol Esters--Immunology --IM; *Peptides--Immunology--IM

Chemical Name: cholesterol ester transfer proteins; (Antibodies, Monoclonal; (Carrier Proteins; (Cholesterol Esters; (Peptides

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08919425 97041286

Differing effects of pancreas-kidney transplantation with systemic versus
portal venous drainage on **cholesterol ester transfer** in
IDDM subjects.

Bagdade JD; Ritter MC; Kitabchi AE; Huss E; Thistlethwaite R; Gabfr O;
Lambeth H

Department of Medicine, Rush Medical College, Chicago, Illinois, USA.

Diabetes Care (UNITED STATES) Oct 1996, 19 (10) p1108-12, ISSN
0149-5992 Journal Code: EAG

Contract/Grant No.: RR-02211, RR, NCRR

Languages: ENGLISH

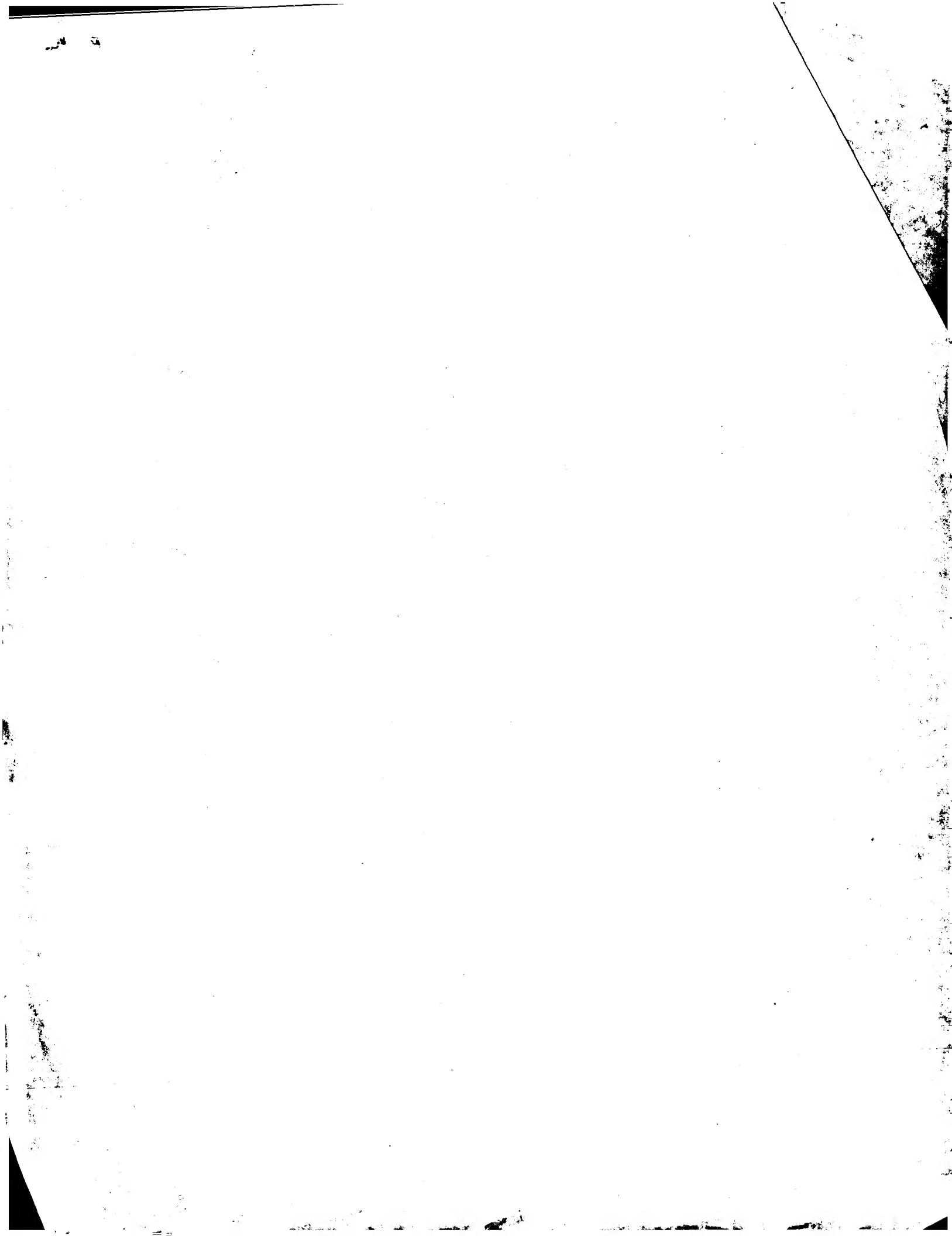
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File 155: MEDLINE(R) 1966-1999/Dec W4
(c) format only 1999 Dialog Corporation
*File 155: Medline updates are complete for 1999.
First update for 2000 will be added in mid-December.
File 55: BIOSIS Previews(R) 1993-1999/Oct W5
(c) 1999 BIOSIS
File 34: SciSearch(R) Cited Ref Sci 1990-1999/Nov W4
(c) 1999 Inst for Sci Info
File 434: SciSearch(R) Cited Ref Sci 1974-1989/Dec
(c) 1998 Inst for Sci Info

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197390		HEPATITIS
1308061	B	
181258	CORE	
2255487	PROTEIN	
S1	547	HEPATITIS(W) B(5N) CORE(5N) PROTEIN
? s antigenic(5n)carrier		
79250		ANTIGENIC
160083	CARRIER	
S2	202	ANTIGENIC(5N)CARRIER
? s s1 and s2		
547	S1	
202	S2	
S3	1	S1 AND S2
? t s3/3,k,ab/1		

3/3,K,AB/1 (Item 1 from file: 34)
DIALOG(R) File 34: SciSearch(R) Cited Ref Sci
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04062731 Genuine Article#: RB857 Number of References: 48
Title: INTRODUCTION OF HETEROLOGOUS EPITOPIES INTO THE N-TERMINAL REGION OF
HEPATITIS-B VIRUS CORE PROTEIN
Author(s): KALININA TI; MAKEEVA IV; KHUDYAKOV YE; SAMOSHIN VV; SMIRNOVA EA;
SEMILETOV YA; PAVLYUCHENKOVA RP; KADOSHNIKOV YP; SMIRNOV VD
Corporate Source: RUSSIAN ACAD SCI, IVANOVSKII INST VIROL/MOSCOW
123098//RUSSIA/
Journal: MOLECULAR BIOLOGY, 1995, V29, N1 (JAN-FEB), P117-124
ISSN: 0026-8933
Language: ENGLISH Document Type: ARTICLE
Abstract: Plasmids pPS1-42, pPS1-5, pPS2-17, and pPS1P-30 were constructed which encode several hybrid proteins containing fragments of the preS region of the hepatitis B virus surface protein. Immunoenzyme analysis and immunoelectron microscopy revealed that introduction of short heterologous sequences into this region does not hinder specific aggregation. The antigenic determinants introduced were exposed on the surface of the hybrid protein, and both the **carrier** and epitopes possessed **antigenic** activity.

Title: INTRODUCTION OF HETEROLOGOUS EPITOPIES INTO THE N-TERMINAL REGION OF
HEPATITIS-B VIRUS CORE PROTEIN
...Abstract: antigenic determinants introduced were exposed on the surface of the hybrid protein, and both the **carrier** and epitopes possessed **antigenic** activity.



86-0459 001 (LOW-DENSITY...
? ds

Set Items Description
S1 2955 CETP OR CHOLESTERYL(W) ESTER(5N) TRANSFER(5N) PROTEIN
S2 1849 HBCAG OR HEPATITIS(W) B(5N) CORE(5N) PROTEIN
S3 0 S1 AND S2
S4 80897 HEPATITIS(W) B
S5 2 S1 AND S4
S6 2 RD (unique items)
? s carrier

S7 160083 CARRIER
? s s1 and s7

2955 S1
160083 S7
S8 616 S1 AND S7
? s conjugat? or fusion or fused or link?

162295 CONJUGAT?
191422 FUSION
48777 FUSED
627305 LINK?
S9 982918 CONJUGAT? OR FUSION OR FUSED OR LINK?
? s s8 and s9

616 S8
982918 S9
S10 51 S8 AND S9
? rd

...examined 50 records (50)
...completed examining records
S11 50 RD (unique items)
? s s11 and py<=1997

Processing

50 S11
28289569 PY<=1997
S12 36 S11 AND PY<=1997
? t s12/3,k,ab/1-36

12/3,K,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155: MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.

09691098 97473500
Sequencing of the cholesteroyl ester transfer
protein 5' regulatory region using artificial transposons.
Williams S; Hayes L; Elsenboss L; Williams A; Andre C; Abramson R;
Thompson JF; Milos PM
Molecular Sciences Department, Pfizer Inc., Groton, CT 06340, USA.
Gene (NETHERLANDS) Sep 15 1997, 197 (1-2) p101-7, ISSN
0378-1119 Journal Code: FOP
Languages: ENGLISH
Document type: JOURNAL ARTICLE

We have isolated and sequenced genomic clones encompassing more than 5 kb of the 5' flanking region of the **cholesteryl ester transfer protein** gene. This region contains multiple Alu repeats, a Mermaid repeat, and an extensive GA repeat, which made sequencing exceedingly difficult. To circumvent the problems that these repeats posed to traditional sequencing methodologies, we employed a novel transposon-facilitated technique, which greatly simplified sequencing of regions that had been difficult to accomplish otherwise. We utilized the artificial transposon, AT-2, a Bluescript derivative containing the dhfr gene and unique primer sites at both ends of the insertion DNA. Integration of the transposon occurred efficiently and covered the entire region of interest. Analysis of the sequence indicates a number of potential regulatory factor binding sites upstream of the previously characterized minimal promoter. The 5.7-kb regulatory region confers significant transcriptional activation in a conditionally transformed mouse hepatocyte line as compared to a minimal 137-bp promoter fragment. In addition, a tetranucleotide repeat of variable length that may provide a useful genetic marker has been identified 2 kb upstream of the **CETP** transcriptional start site.

Sequencing of the **cholesteryl ester transfer protein** 5' regulatory region using artificial transposons.

Sep 15 1997,

... sequenced genomic clones encompassing more than 5 kb of the 5' flanking region of the **cholesteryl ester transfer protein** gene. This region contains multiple Alu repeats, a Mermaid repeat, and an extensive GA repeat...

... that may provide a useful genetic marker has been identified 2 kb upstream of the **CETP** transcriptional start site.

Descriptors: **Carrier Proteins**--Genetics--GE; *DNA Transposable Elements--Genetics--GE; *Regulatory Sequences, Nucleic Acid--Genetics--GE ...; Liver--Cytology--CY; Mice; Minisatellite Repeats; Molecular Sequence Data; Promoter Regions (Genetics)--Genetics--GE; Recombinant Fusion Proteins; Repetitive Sequences, Nucleic Acid--Genetics--GE; Sequence Analysis, DNA; Trans-Activation (Genetics)--Genetics--GE

Chemical Name: cholesterol ester transfer proteins; (**Carrier Proteins**; (DNA Transposable Elements; (Genetic Markers; (Recombinant Fusion Proteins

12/3,K,AB/2 (Item 2 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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09678044 96417308

Structure-function relationships of human **cholesteryl ester transfer protein**: analysis using monoclonal antibodies.

Roy P; MacKenzie R; Hirama T; Jiang XC; Kussie P; Tall A; Rassart E; Milne R

Departement des Sciences Biologiques, Universite du Quebec a Montreal, Canada.

J Lipid Res (UNITED STATES) Jan 1996, 37 (1) p22-34, ISSN 0022-2275 Journal Code: IX3

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Cholesteryl ester transfer protein (CETP), a 476 amino acid glycoprotein, mediates **cholesteryl ester (CE)**, triglyceride, and phospholipid **transfer** among plasma lipoproteins. A monoclonal antibody (mAb), TP2, specific for an epitope within the last 26 amino acids of **CETP** has been shown to block all **CETP**-mediated lipid transfer, apparently by limiting access to lipid-binding sites in the carboxy terminal of **CETP**. A new panel of 16 anti-human **CETP** mAbs has now been used to further probe the structure-function relationships of **CETP**. Of the new mAbs, 9 partially inhibit

carboxyl end.

12/9/91

CETP-mediated CE transfer (24-43%) from HDL to LDL. The corresponding epitopes were mapped within the **CETP** primary structure by the reactivity of the mAbs with **CETP** variants having deletions or amino acid substitutions. Of the 9 new, neutralizing mAbs, 6 are specific for epitopes situated between residues 410-450 and two others for epitopes between residues 184-260 and 332-366, respectively. The epitope of one neutralizing mAb could not be mapped. Therefore, binding of mAbs to epitopes situated in four non-overlapping regions within **CETP** primary structure that are separated by as many as 280 residues can neutralize **CETP**-mediated CE transfer. Epitopes of mAbs that do not influence CE transfer activity map to the regions 184-260, 261-331, and 367-409, respectively. When pairs of mAbs were tested for their abilities to mutually compete for binding to immobilized **CETP**, competition was observed for mAbs specific for epitopes that are distant in **CETP** primary structure. The cross-competition patterns demonstrate that the carboxy terminal 60% of **CETP** adopts a compact structure. Together with previous mutagenesis studies, the data suggests that a carboxy terminal neutral lipid binding domain may be in close proximity to a lipoprotein binding region within native **CETP**.

Structure-function relationships of human **cholesteryl ester transfer protein**: analysis using monoclonal antibodies.

Jan 1996,

Cholesteryl ester transfer protein (CETP), a 476 amino acid glycoprotein, mediates **cholesteryl ester (CE)**, triglyceride, and phospholipid **transfer** among plasma lipoproteins. A monoclonal antibody (mAb), TP2, specific for an epitope within the last 26 amino acids of **CETP** has been shown to block all **CETP**-mediated lipid transfer, apparently by limiting access to lipid-binding sites in the carboxy terminal of **CETP**. A new panel of 16 anti-human **CETP** mAbs has now been used to further probe the structure-function relationships of **CETP**. Of the new mAbs, 9 partially inhibit **CETP**-mediated CE transfer (24-43%) from HDL to LDL. The corresponding epitopes were mapped within the **CETP** primary structure by the reactivity of the mAbs with **CETP** variants having deletions or amino acid substitutions. Of the 9 new, neutralizing mAbs, 6 are...

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... lipid binding domain may be in close proximity to a lipoprotein binding region within native **CETP**.

Descriptors: **Carrier Proteins**--Chemistry--CH; ***Cholesterol Esters**--Metabolism--ME; ***Protein Structure, Tertiary**; **Antibodies, Monoclonal**; **Binding, Competitive**; **Biological Transport**; **Biosensing Techniques**; **Carrier Proteins**--Genetics--GE; **Carrier Proteins**--Immunology--IM; **Carrier Proteins**--Metabolism--ME; **Cells, Cultured**; **Epitope Mapping**; **Mice**; **Models, Molecular**; **Recombinant Fusion Proteins**--Chemistry--CH; **Recombinant Fusion Proteins**--Immunology--IM; **Recombinant Fusion Proteins**--Metabolism--ME; **Structure-Activity Relationship**

Chemical Name: cholesterol ester transfer proteins; (Antibodies, Monoclonal; (**Carrier Proteins**; (**Cholesterol Esters**; (**Recombinant Fusion Proteins**

12/3,K,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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09017400 97176997

Two families of Lowe oculocerebrorenal syndrome with elevated serum HDL cholesterol levels and **CETP** gene mutation.

Asami T; Inano K; Mida T; Kikuchi T; Uchiyama M

Department of Pediatrics, School of Medicine, Niigata University, Japan.

Acta Paediatr (NORWAY) Jan 1997, 86 (1) p41-5, ISSN 0803-5253

Journal Code: BGC

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The oculocerebrorenal syndrome of Lowe (OCRL) is an **X-linked** recessive disorder which is characterized by renal tubular dysfunction, congenital cataracts, and cognitive impairment. In a review article by Charnas et al. (N Engl J Med 1991; 324: 1318-25), hypercholesterolemia, due to elevated high-density lipoprotein cholesterol (HDL-C) levels, was described as being highly prevalent in OCRL patients. This report prompted us to examine three OCRL children in two unrelated families and we confirmed the high prevalence of high serum HDL-C levels in the patients (3/3). In addition, we found that their normal family members also had high serum HDL-C levels (5/7). Analysis of **cholesteryl ester transfer protein** (**CETP**) genes, which are now recognized as one of factors increasing serum HDLC levels, revealed the D442G mutation in exon 15 in 5 of 10 family members (1/3 of OCRL patients and 4/7 healthy family members), and no mutation of intron 14 G(+1)-to-A. The detected D442G mutation may be one of the causes in our two OCRL families; however, further studies, based on larger numbers of subjects, are needed to confirm these findings.

Two families of Lowe oculocerebrorenal syndrome with elevated serum HDL cholesterol levels and **CETP** gene mutation.

Jan 1997,

The oculocerebrorenal syndrome of Lowe (OCRL) is an **X-linked** recessive disorder which is characterized by renal tubular dysfunction, congenital cataracts, and cognitive impairment. In...

... their normal family members also had high serum HDL-C levels (5/7). Analysis of **cholesteryl ester transfer protein** (**CETP**) genes, which are now recognized as one of factors increasing serum HDLC levels, revealed the...

Descriptors: **Carrier Proteins**--Genetics--GE; *Hypercholesterolemia --Genetics--GE; *Lipoproteins, HDL Cholesterol--Blood--BL; *Mutation --Genetics--GE; *Oculocerebrorenal...

Chemical Name: cholesterol ester transfer proteins; (**Carrier Proteins**; (Lipoproteins, HDL Cholesterol

12/3,K,AB/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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08979178 97172455

Evidence that **cholesteryl ester transfer protein**-mediated reductions in reconstituted high density lipoprotein size involve particle fusion.

Rye KA; Hime NJ; Barter PJ

Division of Cardiovascular Services, Royal Adelaide Hospital, Adelaide, South Australia, Australia 5000.

J Biol Chem (UNITED STATES) Feb 14 1997, 272 (7) p3953-60,
ISSN 0021-9258 Journal Code: HIV

Languages: ENGLISH

Document type: JOURNAL ARTICLE

It is well established that **cholesteryl ester transfer protein (CETP)** changes the size of high density lipoproteins (HDL) during incubation in vitro. It has been suggested that HDL.CETP .HDL ternary complex formation is involved in these changes. The present results, which are consistent with CETP changing the size of spherical reconstituted HDL (rHDL) by a mechanism involving **fusion**, support the ternary complex hypothesis. When rHDL containing a core of cholesteryl esters and either three molecules of apolipoprotein (apo) A-I/particle, (A-I)rHDL, or six molecules of apoA-II/particle, (A-II)rHDL, were incubated individually with CETP, their respective diameters decreased from 9.4 to 7.8 nm and from 9.8 to 8.8 nm. The small (A-I)rHDL and (A-II)rHDL contained, respectively, two molecules of apoA-I/particle and four molecules of apoA-II/particle. As all of the rHDL lipids and apolipoproteins were quantitatively recovered at the end of the incubations, it was apparent that there was a 50% increase in the number of particles. This increase in the number of particles can be explained as follows: (i) sequential binding of two rHDL to CETP to generate a ternary complex, (ii) **fusion** of the rHDL in the ternary complex, and (iii) rearrangement of the **fusion** product into three small particles. Various spectroscopic techniques were used to show that the small rHDL were structurally distinct from the original rHDL. These results provide the first evidence that CETP mediates the **fusion** of spherical rHDL.

Evidence that **cholesteryl ester transfer protein**-mediated reductions in reconstituted high density lipoprotein size involve particle fusion.

Feb 14 1997,

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Descriptors: **Carrier Proteins--Chemistry--CH; *Lipoproteins, HDL --Chemistry--CH**

Chemical Name: cholesterol ester transfer proteins; (**Carrier Proteins; (Lipoproteins, HDL; (Phospholipids; (Recombinant Proteins**

12/3,K,AB/5 (Item 5 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

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08938557 97070859

Mouse monoclonal antipeptide antibodies specific for **cholesteryl ester transfer protein (CETP)**.

Thomas AP; Smith AM; Cumming RI; Jones C; Thomas RC; Pleasants KT; Barakat H

Department of Microbiology and Immunology, East Carolina University School of Medicine, Greenville, North Carolina 27858-4354, USA.

Hybridoma (UNITED STATES) Oct 1996, 15 (5) p359-64, ISSN

12/9/99

0272-457X Journal Code: GFS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A synthetic peptide whose amino acid sequence corresponds to residues 131-142 of human **cholesteryl ester transfer protein** (**CETP**) was used as an immunogen to generate a panel of monoclonal antibodies (MAbs) specific for the intact **CETP** molecule. Spleen cells from BALB/c mice immunized with the peptide conjugated with keyhole limpet hemocyanin (KLH) were fused with SP2/0 myeloma cells. Two MAbs that bound fixed peptide in an enzyme-linked immunoabsorbent assay (ELISA) were partially characterized regarding their specificity and biological activity. ATM192 of the IgG1 subclass and J16-14 of the IgG3 subclass were used in a Western blot assay as well as in the ELISA. We have also shown through the use of immunoprecipitation that ATM192 can remove **CETP** enzyme activity from human serum without destroying the enzyme's activity. We have also shown that the antibodies can bind **CETP** from rabbits. The specificity studies and the lack of inhibition of enzymatic activity suggest that the MAbs bind a structural area of the **CETP** molecule not a part of the active binding site of the enzyme. We conclude that these antibodies can be valuable as tools for studying **CETP** levels in human serum as well as in tissue homogenates from rabbits and humans.

Mouse monoclonal antipeptide antibodies specific for **cholesteryl ester transfer protein** (**CETP**).

Oct 1996,

A synthetic peptide whose amino acid sequence corresponds to residues 131-142 of human **cholesteryl ester transfer protein** (**CETP**) was used as an immunogen to generate a panel of monoclonal antibodies (MAbs) specific for the intact **CETP** molecule. Spleen cells from BALB/c mice immunized with the peptide conjugated with keyhole limpet hemocyanin (KLH) were fused with SP2/0 myeloma cells. Two MAbs that bound fixed peptide in an enzyme-linked immunoabsorbent assay (ELISA) were partially characterized regarding their specificity and biological activity. ATM192 of the...

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Descriptors: Antibodies, Monoclonal--Chemistry--CH; *Antibody Specificity ; *Carrier Proteins--Immunology--IM; *Cholesterol Esters--Immunology --IM; *Peptides--Immunology--IM

Chemical Name: cholesterol ester transfer proteins; (Antibodies, Monoclonal; (Carrier Proteins; (Cholesterol Esters; (Peptides

12/3,K,AB/6 (Item 6 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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08902349 97018342

Allelic variation in the gene encoding the **cholesteryl ester transfer protein** is associated with variation in the plasma concentrations of **cholesteryl ester transfer protein**.

McPherson R; Grundy SM; Guerra R; Cohen JC

Center for Human Nutrition, Department of Clinical Nutrition, Dallas, TX 75235-9052, USA.

J Lipid Res (UNITED STATES) Aug 1996, 37 (8) p1743-8, ISSN 0022-2275 Journal Code: IX3

Contract/Grant No.: HL53917, HL, NHLBI; HL29252, HL, NHLBI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The **cholesteryl ester transfer protein** (**CETP**) mediates the **transfer** of cholesteryl esters from high density lipoproteins (HDL) to triglyceride-rich lipoproteins. Mutations that abolish **CETP** function are associated with very high levels of HDL cholesterol, but the effect of more common allelic variation at this locus is less clear. In this study, we have measured plasma **CETP** concentration and plasma HDL cholesterol concentrations in 694 individuals from 106 nuclear families. Robust sibling-pair methods indicated **linkage** between the **CETP** locus and inter-individual variation in plasma **CETP** concentrations. Allelic variation at the **CETP** locus accounted for 20% of the variation in plasma **CETP** concentration. No relation between allelic variation at the **CETP** locus and plasma HDL cholesterol levels was detected. These data indicate that polymorphism in the **CETP** gene confers variation in plasma **CETP** concentration. However, this degree of variation in **CETP** function is not systematically associated with variation in plasma HDL-C concentrations.

Allelic variation in the gene encoding the **cholesteryl ester transfer protein** is associated with variation in the plasma concentrations of **cholesteryl ester transfer protein**.

Aug 1996,

The **cholesteryl ester transfer protein** (**CETP**) mediates the **transfer** of cholesteryl esters from high density lipoproteins (HDL) to triglyceride-rich lipoproteins. Mutations that abolish **CETP** function are associated with very high levels of HDL cholesterol, but the effect of more...

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Descriptors: Alleles; *Carrier Proteins--Blood--BL; *Carrier Proteins--Genetics--GE; *Variation (Genetics)

Chemical Name: cholesterol ester transfer proteins; (Apolipoprotein A-I; (Carrier Proteins; (Lipoproteins, HDL Cholesterol

12/3,K,AB/7 (Item 7 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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08901298 97112972

Human **cholesteryl ester transfer protein** gene proximal promoter contains dietary cholesterol positive responsive elements and mediates expression in small intestine and periphery while predominant liver and spleen expression is controlled by 5'-distal sequences. Cis-acting sequences mapped in transgenic mice.

Oliveira HCF; Chouinard RA; Agellon LB; Bruce C; Ma L; Walsh A; Breslow JL; Tall AR

Division of Molecular Medicine, Department of Medicine, Columbia University, New York, New York 10032, USA.

J Biol Chem (UNITED STATES) Dec 13 1996, 271 (50) p31831-8,

ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: HL 54591, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE

The plasma cholesteryl ester transfer protein (**CETP**) facilitates the transfer of high density lipoprotein cholesteryl esters to other lipoproteins and appears to be a key regulated component of reverse cholesterol transport. Earlier studies showed that a **CETP** transgene containing natural flanking sequences (-3.4 kilobase pairs (kbp) upstream, +2.2 kbp downstream) was expressed in an authentic tissue distribution and induced in liver and other tissues in response to dietary or endogenous hypercholesterolemia. In order to localize the DNA elements responsible for these effects, we prepared transgenic mice expressing six new DNA constructs containing different amounts of natural flanking sequence of the **CETP** gene. Tissue-specific expression and dietary cholesterol response of **CETP** mRNA were determined. The native pattern of predominant expression in liver and spleen with cholesterol induction was shown by a -3.4 (5'), +0.2 (3') kbp transgene, indicating no major contribution of distal 3'-sequences. Serial 5'-deletions showed that a -570 base pairs (bp) transgene gave predominant expression in small intestine with cholesterol induction of **CETP** mRNA in that organ, and a -370 bp transgene gave highest expression in adrenal gland with partial dietary cholesterol induction of **CETP** mRNA and plasma activity. Further deletion to -138 bp 5'-flanking sequence resulted in a transgene that was not expressed in vivo. Both the -3.4 kbp and -138 bp transgenes were expressed when transfected into a cultured murine hepatocyte cell line, but only the former was induced by treating the cells with LDL. When linked to a human apoA-I transgene, the -570 to -138 segment of the **CETP** gene promoter gave rise to a relative positive response of hepatic apoA-I mRNA to the high cholesterol diet in two out of three transgenic lines. Thus, 5'-elements between -3,400 and -570 bp in the **CETP** promoter endow predominant expression in liver and spleen. Elements between -570 and -370 are required for expression in small intestine and some other tissues, and elements between -370 and -138 contribute to adrenal expression. The minimal **CETP** promoter element associated with a positive sterol response in vivo was found in the proximal **CETP** gene promoter between -370 and -138 bp. This region contains a tandem repeat of a sequence known to mediate sterol down-regulation of the HMG-CoA reductase gene, suggesting either the presence of separate positive and negative sterol response elements in this region or the use of a common DNA element for both positive and negative sterol responses.

Human cholesteryl ester transfer protein gene proximal promoter contains dietary cholesterol positive responsive elements and mediates expression in small intestine...

Dec 13 1996,

The plasma cholesteryl ester transfer protein (**CETP**) facilitates the transfer of high density lipoprotein cholesteryl esters to other lipoproteins and appears to be a key regulated component of reverse cholesterol transport. Earlier studies showed that a **CETP** transgene containing natural flanking sequences (-3.4 kilobase pairs (kbp) upstream, +2.2 kbp downstream...).

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... 570 base pairs (bp) transgene gave predominant expression in small intestine with cholesterol induction of **CETP** mRNA in that organ, and a -370 bp transgene gave highest expression in adrenal gland with partial dietary cholesterol induction of **CETP** mRNA and plasma activity. Further deletion to -138 bp 5'-flanking sequence resulted in a...

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Descriptors: Apolipoproteins--Genetics--GE; *Carrier Proteins--Genetics--GE; *Cholesterol Esters--Genetics--GE; *Cholesterol, Dietary--Pharmacology--PD; *Intestine, Small--Metabolism--ME...
Chemical Name: cholesterol ester transfer proteins; (Apolipoprotein A-I; (Apolipoproteins; (Carrier Proteins; (Cholesterol Esters; (Cholesterol, Dietary

12/3,K,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155: MEDLINE(R)
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08810462 96359443

Quantification of cholesteryl ester transfer protein: activity and immunochemical assay.

Glenn KC; Melton MA

Cardiovascular Disease Research Department, Searle Research and Development, Mansanto Company, St. Louis, Missouri 63167, USA.

Methods Enzymol (UNITED STATES) 1996, 263 p339-51, ISSN 0076-6879 Journal Code: MVA

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Quantification of cholesteryl ester transfer protein: activity and immunochemical assay.

1996,

Descriptors: Carrier Proteins--Metabolism--ME; *Enzyme-Linked Immunosorbent Assay; Antibodies, Monoclonal--Immunology--IM; Carrier Proteins--Blood--BL; Carrier Proteins--Immunology--IM; Cholesterol--Metabolism--ME; Cholesterol Esters--Metabolism--ME; Lipoproteins, HDL--Metabolism--ME; Lipoproteins...

Chemical Name: cholesterol ester transfer proteins; (Antibodies, Monoclonal; (Carrier Proteins; (Cholesterol Esters; (Lipoproteins, HDL; (Lipoproteins, LDL; (Cholesterol

12/3,K,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155: MEDLINE(R)
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08806739 96292476

Expression and secretion of rabbit plasma cholesteryl ester transfer protein by Pichia pastoris.

Kotake H; Li Q; Ohnishi T; Ko KW; Agellon LB; Yokoyama S
Lipid and Lipoprotein Research Group, University of Alberta, Edmonton, Canada.

J Lipid Res (UNITED STATES) Mar 1996, 37 (3) p599-605, ISSN 0022-2275 Journal Code: IX3

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The rabbit cholesteryl ester transfer protein (CETP) was expressed in the methylotrophic yeast Pichia pastoris by introducing the CETP cDNA under the control of the methanol-inducible alcohol oxidase promoter. The cDNA was cloned from in vitro amplified cDNA of rabbit liver mRNA. The nucleotide sequence of the cloned cDNA differed slightly from the previously published sequence that changed the amino acid sequence in six residues. Interestingly, five of these replacements are identical to the corresponding residues in human CEPT. In addition, the encoded mature N-terminal sequence was changed from Cys- to Arg-Glu-Phe- to link the CETP sequence to the yeast acid phosphatase signal peptide. The culture medium of the transformed cells induced with 1% methanol contained both cholesteryl ester and triglyceride transfer activity comparable to that of rabbit plasma. Like rabbit plasma, the lipid transfer activity in the medium could be inhibited by monoclonal antibodies that block CE/TG transfer or TG transfer alone. Immunoblot analysis of M(r) = 80 K and minor species of M(r) = 60-100 K. In spite of these differences, the specific transfer activity of the recombinant CETP was indistinguishable from that of rabbit plasma CETP of M(r) = 74 K. N-Glycosidase F treatment converted both the recombinant and plasma CETP to a single species of M(r) = 55 K. Both the plasma and recombinant CETP lost their activity after removal of N-linked carbohydrate and sialic acid. A single 55 K component was found in the cell-lysates. The intracellular form of the recombinant CETP was not modified by N-glycosidase F treatment. In conclusion, the recombinant CETP is synthesized as an inactive polypeptide that is processed and secreted as a functional glycoprotein. In addition, the N-terminal Cys residue of the plasma CETP is not required for its activity.

Expression and secretion of rabbit plasma cholesteryl ester transfer protein by Pichia pastoris.

Mar 1996,

The rabbit cholesteryl ester transfer protein (CETP) was expressed in the methylotrophic yeast Pichia pastoris by introducing the CETP cDNA under the control of the methanol-inducible alcohol oxidase promoter. The cDNA was cloned...

... the encoded mature N-terminal sequence was changed from Cys- to Arg-Glu-Phe- to link the CETP sequence to the yeast acid phosphatase signal peptide. The culture medium of the transformed cells...

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Descriptors: Carrier Proteins--Genetics--GE; *Pichia--Genetics--GE; Amidohydrolases--Metabolism--ME; Blotting, Western; Carrier Proteins--Biosynthesis--BI; Carrier Proteins--Chemistry--CH; Carrier Proteins--Metabolism--ME; Cholesterol Esters--Metabolism--ME; Cloning, Molecular; Culture Media, Conditioned; Gene Expression; Glycosylation...

Chemical Name: Amidohydrolases; (peptide-N4-(N-acetyl-beta-glucosaminyl)asparagine amidase; (cholesterol ester transfer proteins; (Carrier Proteins; (Cholesterol Esters; (Culture Media, Conditioned; (Recombinant Proteins; (Triglycerides

08801302 97008963

Modulation of the activity of the human **cholesteryl ester transfer protein** by carboxylated derivatives. Evidence for 13-cis-retinoic acid as a potent activator of the protein's activity in plasma.

Florentin E; Athias A; Lagrost L

Laboratoire de Biochimie des Lipoproteines, INSERM CJF 93-10, Faculte de Medecine, Dijon, France.

Eur J Biochem (GERMANY) Sep 15 1996, 240 (3) p699-706, ISSN 0014-2956 Journal Code: EMZ

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The influence of palmitic acid, 13-cis-retinoic acid, all-trans-retinoic acid, and all-trans-retinol on the activity of the human **cholesteryl ester transfer protein (CETP)** was evaluated either in total human plasma supplemented with a tracer dose of 3H-labeled cholesteryl-ester-containing high-density lipoprotein sub-fraction 3 ([³H]CE-HDL3), or in reconstituted mixtures containing [³H]CE-HDL3, isolated low-density lipoproteins (LDL), and purified CETP. In reconstituted mixtures, all the carboxylated derivatives increased progressively and significantly the transfer of 3H-labeled cholesteryl esters from [³H]CE-HDL3 towards LDL in the 20-100 microM concentration range. Under identical experimental conditions, CETP activity was only minimally modified in the presence of all-trans-retinol. When present at a concentration of 60, 80, or 100 microM, 13-cis-retinoic acid was a significantly more potent activator of CETP activity than all the other derivatives studied ($P < 0.01$ in all cases). In contrast to observations made with reconstituted mixtures, only 13-cis-retinoic acid, but not palmitic acid, was able to induce a significant, concentration-dependent stimulation of CETP activity in total human plasma. In fact, differences in the ability of 13-cis-retinoic acid and palmitic acid to modulate the plasma cholesteryl ester transfer reaction were linked to their relative affinity for albumin and lipoprotein substrates: fatty-acid-poor albumin reduced CETP activity to a significantly greater extent in reconstituted mixtures containing palmitic acid than in reconstituted mixtures containing 13-cis-retinoic acid ($P < 0.01$ for all the incubation mixtures in the 1-10 g/l albumin concentration range); palmitic acid presented a markedly lower ability to increase the electrophoretic mobility of LDL and HDL fractions in total plasma than 13-cis-retinoic acid. In support of a key role of the negatively charged carboxylic group of 13-cis-retinoic acid in upregulating CETP activity, cholesteryl ester transfer rates correlated positively with the electrophoretic mobility of LDL ($r = 0.98$; $P < 0.0002$) and HDL ($r = 0.96$; $P < 0.0008$) in total plasma supplemented with the carboxylated compound. It is concluded that 13-cis-retinoic acid can upregulate the CETP-mediated cholesteryl ester transfer reaction both in reconstituted mixtures containing isolated lipoproteins and purified CETP, and in total normolipidemic human plasma.

Modulation of the activity of the human **cholesteryl ester transfer protein** by carboxylated derivatives. Evidence for 13-cis-retinoic acid as a potent activator of the...

Sep 15 1996,

... acid, all-trans-retinoic acid, and all-trans-retinol on the activity of the human **cholesteryl ester transfer protein (CETP)** was evaluated either in total human plasma supplemented with a tracer dose of 3H-labeled...

... or in reconstituted mixtures containing [³H]CE-HDL3, isolated low-density lipoproteins (LDL), and purified CETP. In reconstituted mixtures, all the carboxylated derivatives increased progressively and significantly the transfer of 3H...

... CE-HDL3 towards LDL in the 20-100 microM concentration range. Under identical experimental conditions, CETP activity was only minimally modified in the presence of all-trans-retinol. When present at...

... 80, or 100 microM, 13-cis-retinoic acid was a significantly more potent activator of CETP activity than all the other derivatives studied ($P < 0.01$ in all cases). In contrast...

... acid, but not palmitic acid, was able to induce a significant, concentration-dependent stimulation of CETP activity in total human plasma. In fact, differences in the ability of 13-cis-retinoic acid and palmitic acid to modulate the plasma cholesteryl ester transfer reaction were linked to their relative affinity for albumin and lipoprotein substrates: fatty-acid-poor albumin reduced CETP activity to a significantly greater extent in reconstituted mixtures containing palmitic acid than in reconstituted...

... key role of the negatively charged carboxylic group of 13-cis-retinoic acid in upregulating CETP activity, cholesteryl ester transfer rates correlated positively with the electrophoretic mobility of LDL ($r = 0...$

... with the carboxylated compound. It is concluded that 13-cis-retinoic acid can upregulate the CETP -mediated cholesteryl ester transfer reaction both in reconstituted mixtures containing isolated lipoproteins and purified CETP, and in total normolipidemic human plasma.

Descriptors: **Carrier Proteins--Blood--BL;** *Cholesterol Esters --Blood--BL; *Isotretinoin--Pharmacology--PD

Chemical Name: cholesterol ester transfer proteins; (high density lipoprotein-3; (Carrier Proteins; (Cholesterol Esters; (Lipoproteins, HDL; (Lipoproteins, LDL; (Vitamin A; (Tretinoin; (Isotretinoin; (Palmitic Acid

12/3,K,AB/11 (Item 11 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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08697210 96203637

Multilocus genetic determinants of LDL particle size in coronary artery disease families.

Rotter JI; Bu X; Cantor RM; Warden CH; Brown J; Gray RJ; Blanche PJ; Krauss RM; Lusis AJ

Departments of Medicine and Pediatrics, Cedar-Sinai Medical Center, Los Angeles, CA 90048, USA.

Am J Hum Genet (UNITED STATES) Mar 1996, 58 (3) p585-94, ISSN 0002-9297 Journal Code: 3IM

Contract/Grant No.: HL28481, HL, NHLBI; HL18574, HL, NHLBI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Recent interest in atherosclerosis has focused on the genetic determinants of low-density lipoprotein (LDL) particle size, because of (i) the association of small dense LDL particles with a three-fold increased risk for coronary artery disease (CAD) and (ii) the recent report of linkage of the trait to the LDL receptor (chromosome 19). By utilizing nonparametric quantitative sib-pair and relative-pair analysis methods in CAD families, we tested for linkage of a gene or genes controlling LDL particle sizes with the genetic loci for the major apolipoproteins and enzymes participating in lipoprotein metabolism. We confirmed evidence for linkage to the LDL receptor locus ($P=.008$). For six candidate gene loci, including apolipoprotein(apo)B, apoAII, apo(a), apoE-Cl-CII, lipoprotein lipase, and high-density lipoprotein-binding protein, no evidence for linkage was observed by sib-pair linkage analyses (P values ranged from .24 to .81). However, in addition, we did find tentative evidence for linkage with the

apoAI-CIII-IV locus (chromosome 11) ($P=.06$) and significant evidence for linkage of the cholestryl ester transfer protein locus (chromosome 16) ($P=.01$) and the manganese superoxide dismutase locus (chromosome 6) ($P=.001$), thus indicating multilocus determination of this atherogenic trait.

Mar 1996,

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Descriptors: Coronary Disease--Genetics--GE; *Genes--Genetics--GE; *Linkage (Genetics); *Lipoproteins, LDL--Genetics--GE; Adolescence; Adult; Apolipoproteins--Genetics--GE; Base Sequence; Carrier Proteins --Genetics--GE; Coronary Disease--Blood--BL; Genotype; Lipoproteins, LDL --Blood--BL; Lipoproteins, LDL--Chemistry...

Chemical Name: Superoxide Dismutase; (cholesterol ester transfer proteins ; (Apolipoproteins; (Carrier Proteins; (Lipoproteins, LDL; (Receptors , LDL

12/3,K,AB/12 (Item 12 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

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08533973 96114137

Enzyme-linked immunosorbent assay for cholestryl ester transfer protein in human serum.

Sato T; Fukasawa M; Kinoshita M; Arai H; Saeki T; Naraki T; Iwasaki Y; Teramoto T; Takahashi K; Saito Y; et al

Tsukuba Research Laboratories, Ibaraki, Japan.

Clin Chim Acta (NETHERLANDS) Aug 31 1995, 240 (1) p1-9, ISSN 0009-8981 Journal Code: DCC

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Enzyme-linked immunosorbent assay for cholestryl ester transfer protein in human serum.

Aug 31 1995,

Descriptors: Carrier Proteins--Blood--BL; Antibodies, Monoclonal; Cholesterol Esters--Blood--BL; Enzyme-Linked Immunosorbent Assay; Lipids--Blood--BL; Lipoproteins, HDL Cholesterol--Blood--BL

Chemical Name: cholesterol ester transfer proteins; (Antibodies, Monoclonal; (Carrier Proteins; (Cholesterol Esters; (Lipids; (Lipoproteins, HDL Cholesterol

12/3,K,AB/13 (Item 13 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

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08399427 95386727

Alcohol intake modulates the effect of a polymorphism of the cholesteryl ester transfer protein gene on plasma high density lipoprotein and the risk of myocardial infarction.

Fumeron F; Betouille D; Luc G; Behague I; Ricard S; Poirier O; Jemaa R; Evans A; Arveiler D; Marques-Vidal P; et al

INSERM U286 Faculte de Medicine Xavier Bichat, Paris, France.

J Clin Invest (UNITED STATES) Sep 1995, 96 (3) p1664-71, ISSN 0021-9738 Journal Code: HS7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A polymorphism of the CETP gene (CETP/TaqIB) with two alleles B1 (60%) and B2 (40%) has been investigated in relation to lipid variables and the risk of myocardial infarction in a large case-control study (ECTIM) of men aged 25-64. No association was observed between the polymorphism and LDL or VLDL related lipid variables. Conversely, B2 carriers had reduced levels of plasma CETP ($P < 0.0001$) and increased levels of HDL cholesterol ($P < 0.0001$) and of other HDL related lipid variables. The effects of the polymorphism on plasma CETP and HDL cholesterol were independent, suggesting the presence of at least two functional variants linked to B2. A search for these variants on the coding sequence of the CETP gene failed to identify them. The effect of B2 on plasma HDL cholesterol was absent in subjects drinking < 25 grams/d of alcohol but increased commensurably, with higher values of alcohol consumption (interaction: $P < 0.0001$). A similar interaction was not observed for plasma CETP. The odds-ratio for myocardial infarction of B2 homozygotes decreased from 1.0 in nondrinkers to 0.34 in those drinking 75 grams/d or more. These results provide the first demonstration of a gene-environment interaction affecting HDL cholesterol levels and coronary heart disease risk.

Alcohol intake modulates the effect of a polymorphism of the cholesteryl ester transfer protein gene on plasma high density lipoprotein and the risk of myocardial infarction.

Sep 1995,

A polymorphism of the CETP gene (CETP/TaqIB) with two alleles B1 (60%) and B2 (40%) has been investigated in relation to...

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... of alcohol consumption (interaction: $P < 0.0001$). A similar interaction was not observed for plasma CETP. The odds-ratio for myocardial infarction of B2 homozygotes decreased from 1.0 in nondrinkers...

Descriptors: Alcohol Drinking--Metabolism--ME; *Carrier Proteins --Genetics--GE; *Cholesterol Esters--Metabolism--ME; *Lipoproteins, HDL --Blood--BL; *Myocardial Infarction--Epidemiology--EP...
; Adult; Alleles; Analysis of Variance; Base Sequence; Carrier Proteins--Biosynthesis--BI; Case-Control Studies; Introns; Lipoproteins, LDL--Blood--BL; Lipoproteins, VLDL--Blood--BL...

Chemical Name: cholesterol ester transfer proteins; (Carrier Proteins; (Cholesterol Esters; (Lipoproteins, HDL; (Lipoproteins, LDL; (Lipoproteins, VLDL; (Oligodeoxyribonucleotides

12/3,K,AB/14 (Item 14 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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08384995 95341201

Low level quantification of cholesteryl ester transfer protein in plasma subfractions and cell culture media by monoclonal antibody-based immunoassay.

Clark RW; Moberly JB; Bamberger MJ

Department of Cardiovascular and Metabolic Diseases, Pfizer, Inc., Groton, CT 06340, USA.

J Lipid Res (UNITED STATES) Apr 1995, 36 (4) p876-89, ISSN 0022-2275 Journal Code: IX3

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Sensitive immunoradiometric (IRMA) and ELISA assays for cholesteryl ester transfer protein (CETP) have been developed using two different monoclonal antibodies (MAbs). The MAbs were prepared against human plasma CETP and demonstrated specificity by their inhibition of cholesteryl ester transfer activity and by immunoblots of crude plasma fractions and whole media from transfected CHO cells. For these sandwich-type assays, one MAb, 2F8, is used for capture, and the second MAb, 2E7, is iodinated (IRMA) or conjugated with alkaline phosphatase (ELISA) and used for detection. Both assays are linear and provide sensitivities much greater than previously reported. The IRMA allows for the accurate quantification of CETP in the range of 0.5-20 ng/assay (5-200 ng/ml), the ELISA 0.05-5 ng/assay (0.5-50 ng/ml). Using the IRMA, the mean plasma CETP concentration in 44 normolipidemic individuals was determined to be 2.10 +/- 0.36 micrograms/ml; 2.05 +/- 0.33 for males (n = 25) and 2.16 +/- 0.40 for females (n = 19). Values ranged from 1.28 to 2.97 micrograms/ml and CETP mass correlated well with cholesteryl ester transfer activity ($r = 0.913$, n = 23). The distribution of CETP in human plasma was examined both by gel permeation fast protein liquid chromatography (FPLC) and by native gel electrophoresis. For FPLC using agarose resins, a low ionic strength, isotonic buffer system resulted in near total recoveries of CETP, and demonstrated a peak for CETP mass centered at molecular masses of 150 to 180 kilodaltons, larger than that for free monomeric CETP. Native acrylamide gel electrophoresis of plasma from six individuals, followed by 2F8/2E7 sandwich immunoblotting, showed CETP migrating within a size range of 170-220 kilodaltons. This result is consistent with suggestions that plasma CETP is associated with small-sized HDL. Agarose gel electrophoresis showed plasma CETP, as well as purified recombinant CETP, to be prebeta migrating. For determining the concentration of CETP in the media of cultured HepG2 cells, advantage was taken of the high sensitivity of the ELISA. CETP levels were found to increase linearly over the 100-h culture period, reaching 8.0 +/- 0.4 ng/ml (18.0 +/- 1.3 ng/mg cell protein). These sensitive, direct immunoassays for CETP mass should be valuable aids for examining the behavior of CETP in plasma and other complex systems, as well as for studying the synthesis and secretion of CETP by different cells and tissues.

Low level quantification of cholesteryl ester transfer protein in plasma subfractions and cell culture media by monoclonal antibody-based immunoassay.

Apr 1995,

Sensitive immunoradiometric (IRMA) and ELISA assays for cholesteryl ester transfer protein (CETP) have been developed using two different monoclonal antibodies (MAbs). The MAbs were prepared against human plasma CETP and demonstrated specificity by their inhibition of cholesteryl ester transfer activity and by immunoblots of...

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Descriptors: Carrier Proteins--Analysis--AN; *Enzyme-Linked Immunosorbent Assay--Methods--MT; Antibodies, Monoclonal; Carrier Proteins--Immunology--IM; Cells, Cultured; Culture Media; Liver --Metabolism--ME; Mice; Mice, Inbred BALB C...
Chemical Name: cholesterol ester transfer proteins; (Antibodies, Monoclonal; (Carrier Proteins; (Culture Media

12/3, K, AB/15 (Item 15 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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08312221 95263477

Molecular determinants of plasma cholesteryl ester transfer protein binding to high density lipoproteins.

Bruce C; Davidson WS; Kussie P; Lund-Katz S; Phillips MC; Ghosh R; Tall AR

Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York 10032, USA.

J Biol Chem (UNITED STATES) May 12 1995, 270 (19) p11532-42,
ISSN 0021-9258 Journal Code: HIV

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The plasma cholesteryl ester transfer protein (CETP) mediates the transfer of neutral lipids between lipoproteins and is associated with high density lipoproteins (HDL). To understand the mechanism of interaction of CETP with HDL, we studied the binding of pure recombinant CETP to 1-palmitoyl-2-oleoylphosphatidylcholine (POPC)/apoA-I discoidal particles. Separating bound from free CETP using native gradient gel electrophoresis, complexes of CETP with 10-nm hydrodynamic diameter discoidal particles migrated with a diameter of 12-16 nm, compared with approximately 7.5 nm for CETP. At lower ratios of CETP to discs, CETP bound to discs without displacement of apoA-I. CETP alone was unable to generate discoidal complexes. Cross-linking and fluorescence resonance energy transfer experiments indicated that CETP bound to discs as monomers. Cross-linking of CETP to apoA-I in discs suggested proximity of apoA-I and CETP. By negative-stain electron microscopy, discoidal complexes containing CETP and CETP

monoclonal antibody showed localization of antibody molecules to the disc edge, suggesting that **CETP** was bound to the disc edge. The binding of **CETP** to discs of different composition or size was studied. Discs (10-nm Stokes diameter) prepared with either apoA-I or apoA-II had a similar K_d (120 nM). Inclusion of 1 mol % cholestryl oleate, 5 mol % cholesterol, or 6 mol % phosphatidylinositol increased the binding affinity of **CETP** 3-10 times (20-30 nM). In comparison, plasma HDL3 had a K_d of approximately 450 nM. For POPC/apoA-I discs, 10-nm discs bound **CETP** with much higher affinity than smaller 7.8-nm discs (K_d = 1-2 microM). 7.7-nm hydrodynamic diameter POPC/apoA-I spherical particles containing either triolein or cholestryl oleate in their core bound **CETP** with higher affinity (K_d = 50-100 nM) than 7.8-nm POPC/apoA-I discs. Thus, **CETP** appears to bind to the perimeter of discoidal particles, possibly in a process in which flexible segments in apoA-I or apoA-II accommodate **CETP** at the disc edge. The binding of **CETP** to HDL is markedly influenced by overall particle size and shape and by lipid composition, and the increased binding affinity for cholesterol- and cholestryl ester-containing discs suggests a higher affinity of **CETP** for nascent than mature HDL.

Molecular determinants of plasma **cholestryl ester transfer protein** binding to high density lipoproteins.

May 12 1995,

The plasma **cholestryl ester transfer protein** (**CETP**) mediates the **transfer** of neutral lipids between lipoproteins and is associated with high density lipoproteins (HDL). To understand the mechanism of interaction of **CETP** with HDL, we studied the binding of pure recombinant **CETP** to 1-palmitoyl-2-oleoylphosphatidylcholine (POPC)/apoA-I discoidal particles. Separating bound from free **CETP** using native gradient gel electrophoresis, complexes of **CETP** with 10-nm hydrodynamic diameter discoidal particles migrated with a diameter of 12-16 nm, compared with approximately 7.5 nm for **CETP**. At lower ratios of **CETP** to discs, **CETP** bound to discs without displacement of apoA-I. **CETP** alone was unable to generate discoidal complexes. Cross-linking and fluorescence resonance energy transfer experiments indicated that **CETP** bound to discs as monomers. Cross-linking of **CETP** to apoA-I in discs suggested proximity of apoA-I and **CETP**. By negative-stain electron microscopy, discoidal complexes containing **CETP** and **CETP** monoclonal antibody showed localization of antibody molecules to the disc edge, suggesting that **CETP** was bound to the disc edge. The binding of **CETP** to discs of different composition or size was studied. Discs (10-nm Stokes diameter) prepared...

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... increased binding affinity for cholesterol- and cholestryl ester-containing discs suggests a higher affinity of **CETP** for nascent than mature HDL.

Descriptors: **Carrier Proteins--Metabolism--ME**; ***Lipoproteins, HDL--Metabolism--ME...**; **I--Isolation and Purification--IP**; **Apolipoprotein A-I--Metabolism--ME**; **Apolipoprotein A-I--Ultrastructure--UL**; **Carrier Proteins--Isolation and Purification--IP**; **Carrier Proteins**

--Ultrastructure--UL; Cell Line; Cholesterol Esters--Metabolism--ME; Cricetus; Dimyristoylphosphatidylcholine; Hamsters; Kinetics; Lipoproteins, HDL...
Chemical Name: cholesterol ester transfer proteins; (Apolipoprotein A-I; Carrier Proteins; (Cholesterol Esters; (Lipoproteins, HDL; (Liposomes; (Recombinant Proteins; (Dimyristoylphosphatidylcholine

12/3, K, AB/16 (Item 16 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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08287865 95221608

Decreased cholesteryl ester transfer protein (CETP) mRNA and protein and increased high density lipoprotein following lipopolysaccharide administration in human CETP transgenic mice.

Masucci-Magoulas L; Moulin P; Jiang XC; Richardson H; Walsh A; Breslow JL; Tall A

Department of Medicine, College of Physicians and Surgeons, Columbia University, New York 10032, USA.

J Clin Invest (UNITED STATES) Apr 1995, 95 (4) p1587-94, ISSN 0021-9738 Journal Code: HS7

Contract/Grant No.: HL-43165, HL, NHLBI; HL-21006, HL, NHLBI; HL-33714, HL, NHLBI; +

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The plasma cholesteryl ester transfer protein (CETP) mediates the exchange of HDL cholesteryl esters (CE) and VLDL triglycerides leading to catabolism of HDL. There is some evidence that HDL ameliorates the toxicity of LPS, and LPS is known to influence several enzymes affecting HDL metabolism. Therefore, the effects of LPS on CETP and plasma lipoproteins were examined in human CETP transgenic mice. Administration of LPS to mice expressing a CETP transgene linked to its natural flanking sequences (NFR-CETP Tg) resulted in a rapid marked decrease in hepatic CETP mRNA and plasma CETP concentration. Corticosteroid injection produced a similar decrease in hepatic CETP mRNA and adrenalectomy abolished this response to LPS. LPS caused disproportionate reductions in plasma CETP activity compared to mass, and was found to be a potent inhibitor of CETP activity when added directly to plasma. LPS was injected into mice expressing (A) a human apoA-I transgene, (B) apoA-I and NFR-CETP transgenes, or (C) apoA-I and LPS-inducible metallothionein promoter-driven CETP transgenes, producing (A) minimal changes in HDL cholesterol, (B) decreased plasma CETP and increased HDL cholesterol, and (C) increased plasma CETP and decreased HDL cholesterol. Thus, LPS administration produces a profound decrease in hepatic CETP mRNA, primarily as a result of adrenal corticosteroid release. The decrease in plasma CETP activity after LPS administration may reflect both this effect as well as a direct interaction between CETP and LPS. The decrease of CETP in response to LPS has major effects on HDL levels, and may represent an adaptive response to preserve or increase HDL and thereby modify the response to LPS.

Decreased cholesteryl ester transfer protein (CETP) mRNA and protein and increased high density lipoprotein following lipopolysaccharide administration in human CETP transgenic mice.

Apr 1995,

The plasma cholesteryl ester transfer protein (CETP) mediates the exchange of HDL cholesteryl esters (CE) and VLDL triglycerides leading to catabolism of...

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Descriptors: **Carrier Proteins**--Biosynthesis--BI; *Cholesterol Esters--Metabolism--ME; *Gene Expression Regulation--Drug Effects--DE; *Lipopolysaccharides--Pharmacology...
; **Carrier Proteins**--Blood--BL; **Carrier Proteins**--Genetics--GE; Cell Nucleus--Metabolism--ME; Cholesterol--Analysis--AN; Lipids--Blood--BL; Liver--Metabolism...

Chemical Name: cholesterol ester transfer proteins; (**Carrier Proteins**; (Cholesterol Esters; (Lipids; (Lipopolysaccharides; (Lipoproteins, HDL; (RNA, Messenger; (Cholesterol

12/3, K, AB/17 (Item 17 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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08214063 94307325

Effect of adiposity on plasma lipid transfer protein activities: a possible link between insulin resistance and high density lipoprotein metabolism.

Dullaart RP; Sluiter WJ; Dikkeschei LD; Hoogenberg K; Van Tol A.
Department of Endocrinology, State University Hospital Groningen, The Netherlands.

Eur J Clin Invest (ENGLAND) Mar 1994, 24 (3) p188-94, ISSN 0014-2972 Journal Code: EN3

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The mechanisms responsible for the decreased high density lipoprotein (HDL) cholesterol levels associated with obesity and insulin resistance are not well understood. Lecithin: cholesterol acyltransferase (LCAT) and cholesterol ester transfer protein (**CETP**) are key factors in the esterification of cholesterol in HDL and the subsequent transfer of cholestrylyl ester towards apolipoprotein B-containing lipoproteins. Phospholipid transfer protein (PLTP) may be involved in the regulation of HDL particle size. We therefore measured the activities of LCAT, **CETP** and PLTP using exogenous substrate assays, as well as lipids, lipoproteins, insulin and C-peptide in fasting plasma from eight healthy obese men (body mass index > 27 kg m⁻²) and 24 non-obese subjects. The obese men had lower levels of HDL cholesterol (P < 0.05) and higher levels of plasma triglycerides (P < 0.05), insulin (P < 0.05) and C-peptide (P < 0.01), as compared to the quartile of subjects with the lowest body mass index (BMI < 22.4 kg m⁻²). **CETP** and PLTP activities were elevated in the obese men by 35% (P < 0.01) and by 15% (P < 0.05), respectively. LCAT activity was comparable among the quartiles. Linear regression analysis showed that **CETP** activity was positively correlated with body mass index (P < 0.02), fasting blood glucose (P <

0.05) and plasma C-peptide ($P < 0.05$). PLTP activity was positively related to body mass index ($P < 0.01$), waist to hip circumference ratio ($P < 0.001$), as well as to fasting blood glucose ($P < 0.05$) and plasma C-peptide ($P < 0.05$). (ABSTRACT TRUNCATED AT 250 WORDS)

Effect of adiposity on plasma lipid transfer protein activities: a possible link between insulin resistance and high density lipoprotein metabolism.

Mar 1994,

... insulin resistance are not well understood. Lecithin: cholesterol acyltransferase (LCAT) and cholesterol ester transfer protein (CETP) are key factors in the esterification of cholesterol in HDL and the subsequent transfer of cholestryl ester towards apolipoprotein B-containing lipoproteins. Phospholipid transfer protein (PLTP) may be involved in the regulation of HDL particle size. We therefore measured the activities of LCAT, CETP and PLTP using exogenous substrate assays, as well as lipids, lipoproteins, insulin and C-peptide...

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Descriptors: Carrier Proteins--Blood--BL; *Insulin Resistance; *Lipoproteins, HDL--Metabolism--ME; *Membrane Proteins--Blood--BL; *Obesity --Metabolism...

Chemical Name: Sterol O-Acyltransferase; (cholesterol ester transfer proteins; (phospholipid exchange proteins; (Carrier Proteins; (Lipids ; (Lipoproteins, HDL; (Membrane Proteins

12/3, K, AB/18 (Item 18 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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08162618 94199821

Two-site enzyme immunoassay of cholestryl ester transfer protein with monoclonal and oligoclonal antibodies.

Mezdour H; Kora I; Parra HJ; Tartar A; Marcel YL; Fruchart JC
Institut Pasteur de Lille, Serlia et Inserm U-325, France.

Clin Chem (UNITED STATES) Apr 1994, 40 (4) p593-7, ISSN
0009-9147 Journal Code: DBZ

Languages: ENGLISH

Document type: JOURNAL ARTICLE

We developed a sandwich-type enzyme immunoassay to measure cholestryl ester transfer protein (CETP) mass in human plasma. A specific monoclonal antibody (TP-4) that recognizes an epitope located in the C-terminal domain was used for antigen capture and an anti-CETP peptide antibody directed against the 290-306 residue was used for detection. Bound antibodies were revealed with an antibody-peroxidase conjugate specific for rabbit IgG. The presence of 10 mL/L Triton X-100 in the incubation buffer increased antigen exposure of CETP in plasma. The curves for CETP in standard plasma and partially purified CETP were parallel. This technique is rapid (results within 6 h), accurate, precise (mean intra- and interassay CVs 3.6% and 8.4%, respectively), and simple to perform. Assay sensitivity is at microgram concentrations, with a working range of 20-200 micrograms/L. In 40 normolipidemic healthy subjects, the mean CETP concentration in plasma was $1.1 \pm 0.4 \text{ mg/L}$. A strong correlation between CETP concentration and CETP activity ($r = 0.91$, $n = 42$) was observed. In plasma, the bulk of CETP was found in high-density lipoprotein fractions. Therefore, this assay may be a useful tool for investigations of

CETP and its significance in relevant diseases.

Two-site enzyme immunoassay of **cholesteryl ester transfer protein** with monoclonal and oligoclonal antibodies.

Apr 1994,

We developed a sandwich-type enzyme immunoassay to measure **cholesteryl ester transfer protein** (**CETP**) mass in human plasma. A specific monoclonal antibody (TP-4) that recognizes an epitope located in the C-terminal domain was used for antigen capture and an anti-**CETP** peptide antibody directed against the 290-306 residue was used for detection. Bound antibodies were revealed with an antibody-peroxidase conjugate specific for rabbit IgG. The presence of 10 mL/L Triton X-100 in the incubation buffer increased antigen exposure of **CETP** in plasma. The curves for **CETP** in standard plasma and partially purified **CETP** were parallel. This technique is rapid (results within 6 h), accurate, precise (mean intra- and...
... a working range of 20-200 micrograms/L. In 40 normolipidemic healthy subjects, the mean **CETP** concentration in plasma was 1.1 +/- 0.4 mg/L. A strong correlation between **CETP** concentration and **CETP** activity ($r = 0.91$, $n = 42$) was observed. In plasma, the bulk of **CETP** was found in high-density lipoprotein fractions. Therefore, this assay may be a useful tool for investigations of **CETP** and its significance in relevant diseases.

Descriptors: Antibodies; *Antibodies, Monoclonal; *Carrier Proteins --Blood--BL; *Immunoenzyme Techniques; Antibody Specificity; Blood Preservation; Carrier Proteins--Immunology--IM; Epitopes--Immunology --IM; Immunoenzyme Techniques--Statistical and Numerical Data--SN; Microchemistry; Octoxynol...

Chemical Name: cholesterol ester transfer proteins; (Antibodies; (Antibodies, Monoclonal; (Carrier Proteins; (Epitopes; (Peptide Fragments; (Octoxynol

12/3, K, AB/19 (Item 19 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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08133346 95196306

Competitive enzyme-linked immunosorbent assay of the human **cholesteryl ester transfer protein** (**CETP**).

Guyard-Dangremont V; Lagrost L; Gambert P; Lallement C
Laboratoire de Biochimie des Lipoproteines, INSERM CJF 93-10, Faculte de Medecine, Dijon, France.

Clin Chim Acta (NETHERLANDS) Dec 16 1994, 231 (2) p147-60,
ISSN 0009-8981 Journal Code: DCC

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The present report describes the first competitive enzyme-linked immunosorbent assay (ELISA) for the **cholesteryl ester transfer protein** (**CETP**), an enzyme playing an important role in lipoprotein metabolism. This assay was developed with well-characterized TP1 anti-**CETP** monoclonal antibodies. The sensitivity of the ELISA assay was comparable with the sensitivity of the previously described radioimmunoassays since 1 ng of **CETP** per microwell of the immunoplate could be detected. Intra- and inter-assay coefficients of variation were 4% and 6%, respectively. This enzyme immunoassay provides a specific, sensitive and reproducible method for measuring **CETP** concentrations in various biological samples. Within normolipidemic subjects, the mean (+/- S.D.) of the plasma **CETP** concentration was 2.77 (+/- 0.59) micrograms/ml with a range of 1.87 to 4.23 micrograms/ml. When plasmas were supplemented with fatty acid-free albumin, the positive correlation observed between plasma **CETP** mass and **CETP** activity was improved, suggesting that plasma non-esterified fatty acids could play a role in modulating the activity of the **cholesteryl ester transfer protein**. When applied to

the study of the binding of CETP to lipoprotein substrates, the enzyme immunoassay revealed that the experimental protocol used to separate lipoprotein fractions can have a great influence on the plasma distribution of CETP.

Competitive enzyme-linked immunosorbent assay of the human cholesteryl ester transfer protein (CETP).

Dec 16 1994,

The present report describes the first competitive enzyme-linked immunosorbent assay (ELISA) for the cholesteryl ester transfer protein (CETP), an enzyme playing an important role in lipoprotein metabolism. This assay was developed with well-characterized TPI anti-CETP monoclonal antibodies. The sensitivity of the ELISA assay was comparable with the sensitivity of the previously described radioimmunoassays since 1 ng of CETP per microwell of the immunoplate could be detected. Intra- and inter-assay coefficients of variation...

... and 6%, respectively. This enzyme immunoassay provides a specific, sensitive and reproducible method for measuring CETP concentrations in various biological samples. Within normolipidemic subjects, the mean (+/- S.D.) of the plasma CETP concentration was 2.77 (+/- 0.59) micrograms/ml with a range of 1.87 to...

... When plasmas were supplemented with fatty acid-free albumin, the positive correlation observed between plasma CETP mass and CETP activity was improved, suggesting that plasma non-esterified fatty acids could play a role in modulating the activity of the cholesteryl ester transfer protein. When applied to the study of the binding of CETP to lipoprotein substrates, the enzyme immunoassay revealed that the experimental protocol used to separate lipoprotein fractions can have a great influence on the plasma distribution of CETP.

Descriptors: Carrier Proteins--Blood--BL...; Resins--Metabolism--ME ; Antibodies, Monoclonal; Apolipoproteins--Blood--BL; Apolipoproteins --Metabolism--ME; Blood Proteins--Metabolism--ME; Carrier Proteins --Isolation and Purification--IP; Cholesterol Esters--Blood--BL; Chromatography, Affinity--Methods--MT; Enzyme-Linked Immunosorbent Assay; Glycoproteins--Blood--BL; Lipids--Blood--BL; Mice; Sensitivity and Specificity; Triglycerides--Blood--BL...

Chemical Name: cholesterol ester transfer proteins; (Anion Exchange Resins; (Antibodies, Monoclonal; (Apolipoproteins; (Blood Proteins; (Carrier Proteins; (Cholesterol Esters; (Glycoproteins; (Lipids; (Triglycerides; (Mono Q

12/3, K, AB/20 (Item 20 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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08079383 95096086

Co-expression of cholesteryl ester transfer protein and defective apolipoprotein E in transgenic mice alters plasma cholesterol distribution. Implications for the pathogenesis of type III hyperlipoproteinemia.

Fazio S; Marotti KR; Lee YL; Castle CK; Melchior GW; Rall SC Jr
Gladstone Institute of Cardiovascular Disease, University of California,
San Francisco 94141.

J Biol Chem (UNITED STATES) Dec 23 1994, 269 (51) p32368-72,
ISSN 0021-9258 Journal Code: HIV

Contract/Grant No.: HL-47660, HL, NHLBI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Despite the definite etiologic link between apolipoprotein (apo) E mutations and type III hyperlipoproteinemia (HLP), it is not clear what

additional factors are involved in the development of florid hyperlipidemia and how to explain the wide variability in the expression of the hyperlipidemic phenotype in carriers of receptor binding-defective apoE variants. The present study was designed to determine whether the overexpression of **cholesteryl ester transfer protein** (**CETP**), a plasma protein that transfers cholesteryl esters from the high density lipoproteins (HDL) to the very low density lipoproteins (VLDL) and whose activity is increased in hyperlipidemic states, plays a role in the development of hyperlipidemia and beta-VLDL accumulation in type III HLP. We produced double-transgenic mice that co-expressed high levels of simian **CETP** and either high or low levels of a human receptor binding-defective apoE variant, apoE(Cys-142). We previously reported that apoE(Cys-142) high-expresser mice showed spontaneous hyperlipidemia and accumulation of beta-VLDL, whereas the low-expresser mice showed only a modest increase in VLDL cholesterol. Co-expression of **CETP** induced a massive transfer of cholesteryl esters from the HDL to the VLDL in both lines of double-transgenic mice. As a result, HDL cholesterol and apoA-I levels were reduced to about 50% of normal, VLDL cholesterol increased 2.5-fold, and the cholesteryl ester content of VLDL reached values similar to those observed in human beta-VLDL. The ratio of defective to normal apoE in VLDL was unaffected by **CETP** co-expression and was higher in animals expressing high apoE levels. Finally, in spite of an increased accumulation of beta-VLDL in the high-expresser mice, the VLDL of the low-expresser mice maintained pre-beta mobility upon co-expression of **CETP**. The results of this study demonstrate that the ratio of defective to normal apoE on the VLDL, rather than the cholesteryl ester content of VLDL, is the major factor determining the development of severe hyperlipidemia and the formation and accumulation of beta-VLDL in type III HLP.

Co-expression of **cholesteryl ester transfer protein** and defective apolipoprotein E in transgenic mice alters plasma cholesterol distribution. Implications for the pathogenesis...

Dec 23 1994,

Despite the definite etiologic link between apolipoprotein (apo) E mutations and type III hyperlipoproteinemia (HLP), it is not clear what...

... binding-defective apoE variants. The present study was designed to determine whether the overexpression of **cholesteryl ester transfer protein** (**CETP**), a plasma protein that transfers cholesteryl esters from the high density lipoproteins (HDL) to the very low density...

... type III HLP. We produced double-transgenic mice that co-expressed high levels of simian **CETP** and either high or low levels of a human receptor binding-defective apoE variant, apoE...

... the low-expresser mice showed only a modest increase in VLDL cholesterol. Co-expression of **CETP** induced a massive transfer of cholesteryl esters from the HDL to the VLDL in both...

... human beta-VLDL. The ratio of defective to normal apoE in VLDL was unaffected by **CETP** co-expression and was higher in animals expressing high apoE levels. Finally, in spite of...

... the VLDL of the low-expresser mice maintained pre-beta mobility upon co-expression of **CETP**. The results of this study demonstrate that the ratio of defective to normal apoE on...

Descriptors: Apolipoproteins E--Genetics--GE; *Carrier Proteins --Genetics--GE; *Hyperlipoproteinemia--Etiology--ET; *Lipoproteins, HDL Cholesterol--Blood--BL; *Lipoproteins, VLDL Cholesterol--Blood...; Apolipoproteins E--Metabolism--ME; Carrier Proteins--Metabolism--ME; Hyperlipoproteinemia--Blood--BL; Mice; Mice, Inbred C57BL; Mice, Transgenic; Triglycerides--Blood--BL

Chemical Name: cholesterol ester transfer proteins; (Apolipoproteins E; (Carrier Proteins; (Lipoproteins, HDL Cholesterol; (Lipoproteins, VLDL

12/3,K,AB/21 (Item 21 from file: 155)
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08062194 95071990

Intraperitoneal insulin therapy corrects abnormalities in cholestryl ester transfer and lipoprotein lipase activities in insulin-dependent diabetes mellitus.

Bagdade JD; Dunn FL; Eckel RH; Ritter MC

Department of Medicine, Rush Medical College, Chicago, Ill.

Arterioscler Thromb (UNITED STATES) Dec 1994, 14 (12) p1933-9,
ISSN 1049-8834 Journal Code: AZ1

Contract/Grant No.: R01 DK 43227, DK, NIDDK

Languages: ENGLISH

Document type: CLINICAL TRIAL; JOURNAL ARTICLE

Patients with insulin-dependent diabetes mellitus (IDDM) have proatherogenic disturbances in cholestryl ester transfer (CET) despite intensive subcutaneous insulin therapy (ISC). Since CET is activated by insulin-sensitive lipoprotein lipase (LPL), which normally increases postprandially, we queried whether iatrogenic hyperinsulinism from ISC stimulated LPL and CET by studying well-controlled IDDM patients after ISC and then 6 months after lowering systemic insulin levels by intraperitoneal (IP) insulin delivery. Although glycemic control (HbA1c IDDM, 6.9 +/- 1.7%; control, 4.5% to 8%) was excellent during ISC, CET was accelerated ($P < .001$) and both systemic insulin levels and LPL specific activity were increased ($P < .05$). Following IP, basal systemic insulin levels declined by more than one half (ISC, 8.22 +/- 6.5 versus IP, 2.77 +/- 2.4 microU/mL; mean +/- SD; $P < .025$), and both LPL and CET activities returned to normal. Plasma triglyceride, cholesterol, high-density lipoprotein-2 (HDL2) cholesterol, HDL3 cholesterol, **cholestryl ester transfer protein mass, and glycemic control (HbA1c, 6.3 +/- 0.8%) were unchanged and remained normal. These findings indicate that ISC is associated with high levels of basal CET and LPL. These alterations both appear to be closely linked to iatrogenic hyperinsulinemia resulting from ISC. The fact that they are both reversed when systemic insulin levels are reduced by IP suggests that insulin, acting through LPL, influences the nature of the interaction of the lipoproteins engaged in CET.** (ABSTRACT TRUNCATED AT 250 WORDS)

Dec 1994,

... activities returned to normal. Plasma triglyceride, cholesterol, high-density lipoprotein-2 (HDL2) cholesterol, HDL3 cholesterol, **cholestryl ester transfer protein mass, and glycemic control (HbA1c, 6.3 +/- 0.8%) were unchanged and remained normal. These...**

... with high levels of basal CET and LPL. These alterations both appear to be closely linked to iatrogenic hyperinsulinemia resulting from ISC. The fact that they are both reversed when systemic...

Descriptors: **Carrier Proteins--Blood--BL; *Cholesterol Esters --Blood--BL; *Diabetes Mellitus, Insulin-Dependent--Blood--BL; *Diabetes Mellitus...**

Chemical Name: Lipoprotein Lipase; (cholesterol ester transfer proteins; (Blood Glucose; (Carrier Proteins; (Cholesterol Esters; (Hemoglobin A, Glycosylated; (Insulin

12/3,K,AB/22 (Item 22 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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07988324 94356673

Lipoprotein Lp(a) and CETP (cholesterol ester transfer protein): contribution of transgenic mice]

La lipoproteine Lp(a) et la CETP (proteine de transfert des esters de cholesterol): apports des souris transgeniques.

Chapman J; Guerin M

INSERM Unite 321, Hopital de la Pitie, Paris.

Bull Acad Natl Med (FRANCE) Mar 1994, 178 (3) p427-34;
discussion 434-6, ISSN 0001-4079 Journal Code: B8G

Languages: FRENCH Summary Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL English
Abstract

Lipoprotein Lp(a) is a pluri-molecular complex rich in cholesterol and composed of an LDL (low-density lipoprotein) particle to which is attached a large glycoprotein, apolipoprotein(a) (apo(a)). Numerous epidemiological studies have established a strong correlation between plasma levels of Lp(a) and the premature development of atherosomatous vascular disease in man, an association which has subsequently been confirmed by the detection of Lp(a) in human atherosclerotic plaques. Furthermore, a marked structural resemblance has been demonstrated between apo(a) and plasminogen, a key protein of the fibrinolytic system and responsible for dissolution of blood clots. This discovery has provided evidence, for the first time, that Lp(a) might constitute an important link between atherosclerosis and thrombosis. Intense research effort is now underway to provide further understanding of (I) the structural organisation of the Lp(a) particle; (II) the molecular genetics of apo(a); (III) the processes involved in the synthesis, assembly intravascular metabolism and degradation of Lp(a) and apo(a); (IV) the nature of the interactions of Lp(a) and apo(a) with cellular and non-cellular components of the arterial wall; (V) the role of Lp(a) in fibrinolysis, and (VI) the relationship between Lp(a) and certain metabolic disorders such as familial hypercholesterolemia. These fascinating questions will be examined in the light of studies of different models of transgenic mice expressing human apo(a) alone, or both apo(a) and apo B100. In man, CETP assures the transfer of cholestryll ester from high-density lipoproteins (HDL) to lipoproteins containing apo-B, and notably VLDL, IDL and LDL. (ABSTRACT TRUNCATED AT 250 WORDS)

Lipoprotein Lp(a) and CETP (cholesterol ester transfer protein): contribution of transgenic mice]

La lipoproteine Lp(a) et la CETP (proteine de transfert des esters de cholesterol): apports des souris transgeniques.

Mar 1994,

... discovery has provided evidence, for the first time, that Lp(a) might constitute an important link between atherosclerosis and thrombosis. Intense research effort is now underway to provide further understanding of ...

...mice expressing human apo(a) alone, or both apo(a) and apo B100. In man, CETP assures the transfer of cholestryll ester from high-density lipoproteins (HDL) to lipoproteins containing apo...

Descriptors: Carrier Proteins--Genetics--GE; *Cholesterol Esters --Genetics--GE; *Lipoprotein(a)--Genetics--GE; *Mice, Transgenic--Genetics --GE; Atherosclerosis--Blood--BL; Atherosclerosis--Genetics--GE; Carrier Proteins--Chemistry--CH; Cholesterol Esters--Chemistry--CH; Lipoprotein(a)--Chemistry--CH; Mice

Chemical Name: cholesterol ester transfer proteins; (Carrier Proteins; (Cholesterol Esters; (Lipoprotein(a)

12/3,K,AB/23 (Item 23 from file: 155)
DIALOG(R) File 155: MEDLINE(R)

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07933604 94274198

Linkage analysis of the genetic determinants of high density lipoprotein concentrations and composition: evidence for involvement of the

apolipoprotein A-II and cholesteryl ester transfer protein loci.

Bu X; Warden CH; Xia YR; De Meester C; Puppione DL; Teruya S; Lokengard B; Daneshmand S; Brown J; Gray RJ; et al
Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, CA 90048.

Hum Genet (GERMANY) Jun 1994, 93 (6) p639-48, ISSN 0340-6717

Journal Code: GED

Contract/Grant No.: HL42481, HL, NHLBI; HL28481, HL, NHLBI; DK07426, DK, NIDDK; +

Languages: ENGLISH

Document type: JOURNAL ARTICLE

We have tested for evidence of linkage between the genetic loci determining concentrations and composition of plasma high density lipoproteins (HDL) with the genes for the major apolipoproteins and enzymes participating in lipoprotein metabolism. These genes include those encoding various apolipoproteins (apo), including apoA-I, apoA-II, apoA-IV, apoB, apoC-I, apoC-II, apoC-III, apoE, and apo(a), cholesteryl ester transfer protein (CETP), HDL-binding protein, lipoprotein lipase, and the low density lipoprotein (LDL) receptor. Polymorphisms of these genes, and nearby highly polymorphic simple sequence repeat markers, were examined by quantitative sib-pair linkage analysis in 30 coronary artery disease families consisting of a total of 366 individuals. Evidence for linkage was observed between a marker locus D16S313 linked to the CETP locus and a locus determining plasma HDL-cholesterol concentration ($P = 0.002$), and the genetic locus for apoA-II and a locus determining the levels of the major apolipoproteins of HDL, apoA-I and apoA-II ($P = 0.009$ and 0.02 , respectively). HDL level was also influenced by the variation at the apo(a) locus on chromosome 6 ($P = 0.02$). Thus, these data indicate the simultaneous involvement of at least two different genetic loci in the determination of the levels of HDL and its associated lipoproteins.

Linkage analysis of the genetic determinants of high density lipoprotein concentrations and composition: evidence for involvement of the apolipoprotein A-II and cholesteryl ester transfer protein loci.

Jun 1994,

We have tested for evidence of linkage between the genetic loci determining concentrations and composition of plasma high density lipoproteins (HDL) with...

...apoA-II, apoA-IV, apoB, apoC-I, apoC-II, apoC-III, apoE, and apo(a), cholesteryl ester transfer protein (CETP), HDL-binding protein, lipoprotein lipase, and the low density lipoprotein (LDL) receptor. Polymorphisms of these genes, and nearby highly polymorphic simple sequence repeat markers, were examined by quantitative sib-pair linkage analysis in 30 coronary artery disease families consisting of a total of 366 individuals. Evidence for linkage was observed between a marker locus D16S313 linked to the CETP locus and a locus determining plasma HDL-cholesterol concentration ($P = 0.002$), and the genetic...

Descriptors: Apolipoprotein A-II--Genetics--GE; *Carrier Proteins --Genetics--GE; *Linkage (Genetics); *Lipoproteins, HDL--Genetics--GE

Gene Symbol: CETP; apoA-II

Chemical Name: cholesterol ester transfer proteins; (Apolipoprotein A-II; (Apolipoproteins; (Carrier Proteins; (Lipoproteins, HDL

12/3,K,AB/24 (Item 24 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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07551825 93264424

Human plasma cholesteryl ester transfer protein

consists of a mixture of two forms reflecting variable glycosylation at asparagine 341.

Stevenson SC; Wang S; Deng L; Tall AR

Department of Medicine, College of Physicians and Surgeons of Columbia University, New York, New York 10032.

Biochemistry (UNITED STATES) May 18 1993, 32 (19) p5121-6,
ISSN 0006-2960 Journal Code: A0G

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Plasma cholesteryl ester transfer protein (CETP) mediates the transfer of neutral lipids and phospholipids between the plasma lipoproteins. The deduced M(r) of the CETP polypeptide from the cDNA is 53,000, but in sodium dodecyl sulfate (SDS) gels plasma CETP appears as a broad band containing two different molecular forms of M(r) 65,000-71,000. The purpose of this study was to see if variable N-linked glycosylation could explain the microheterogeneity of CETP. Recombinant CETP (rCETP), derived from stable expression of the CETP cDNA in Chinese hamster ovary (CHO) cells, appeared as a protein doublet comparable to plasma CETP. Digestion of plasma or rCETP with N-glycosidase F (glyco F, to remove N-linked carbohydrates) resulted in the formation of a lower M(r) doublet in which the bottom band approximated the M(r) of the CETP polypeptide. Metabolic labeling of the rCETP with [3H]mannose and [3H]glucosamine, followed by digestion with glyco F, suggested that the top band of the doublet contained residual N-linked carbohydrates resistant to glyco F digestion. To explore this hypothesis further, each of the four potential N-linked glycosylation sites of CETP (at amino acid positions 88, 240, 341, and 396) was eliminated by mutagenesis of asparagine to glutamine. The wild-type (WT) and mutant CETP cDNAs were transiently expressed in COS-7 cells. Each mutant CETP showed a lower M(r) than WT, indicating that all four sites were occupied by N-linked carbohydrate. (ABSTRACT TRUNCATED AT 250 WORDS)

Human plasma cholesteryl ester transfer protein consists of a mixture of two forms reflecting variable glycosylation at asparagine 341.

May 18 1993,

Plasma cholesteryl ester transfer protein (CETP) mediates the transfer of neutral lipids and phospholipids between the plasma lipoproteins. The deduced M(r) of the CETP polypeptide from the cDNA is 53,000, but in sodium dodecyl sulfate (SDS) gels plasma CETP appears as a broad band containing two different molecular forms of M(r) 65,000-71,000. The purpose of this study was to see if variable N-linked glycosylation could explain the microheterogeneity of CETP. Recombinant CETP (rCETP), derived from stable expression of the CETP cDNA in Chinese hamster ovary (CHO) cells, appeared as a protein doublet comparable to plasma CETP. Digestion of plasma or rCETP with N-glycosidase F (glyco F, to remove N-linked carbohydrates) resulted in the formation of a lower M(r) doublet in which the bottom band approximated the M(r) of the CETP polypeptide. Metabolic labeling of the rCETP with [3H]mannose and [3H]glucosamine, followed by digestion with glyco F, suggested that the top band of the doublet contained residual N-linked carbohydrates resistant to glyco F digestion. To explore this hypothesis further, each of the four potential N-linked glycosylation sites of CETP (at amino acid positions 88, 240, 341, and 396) was eliminated by mutagenesis of asparagine to glutamine. The wild-type (WT) and mutant CETP cDNAs were transiently expressed in COS-7 cells. Each mutant CETP showed a lower M(r) than WT, indicating that all four sites were occupied by N-linked carbohydrate. (ABSTRACT TRUNCATED AT 250 WORDS)

Descriptors: Asparagine--Metabolism--ME; *Carrier Proteins--Blood--BL; Base Sequence; Carrier Proteins--Chemistry--CH; Carrier Proteins--Genetics--GE; CHO Cells; Glycoside Hydrolases--Metabolism--ME; Glycosylation; Hamsters; Molecular Sequence Data; Molecular...

Chemical Name: Glycoside Hydrolases; (Neuraminidase; (cholesterol ester

transfer proteins; (Carrier Proteins; (Recombinant Proteins;
(Asparagine

12/3, K, AB/25 (Item 25 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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07519354 93207594

Composition of human low density lipoprotein: effects of postprandial triglyceride-rich lipoproteins, lipoprotein lipase, hepatic lipase and cholestrylo ester transfer protein.

Karpe F; Tornvall P; Olivecrona T; Steiner G; Carlson LA; Hamsten A
King Gustaf V Research Institute, Karolinska Hospital, Stockholm, Sweden.
Atherosclerosis (NETHERLANDS) Jan 4 1993, 98 (1) p33-49, ISSN
0021-9150 Journal Code: 95X

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A preponderance of small, dense low density lipoprotein (LDL) particles has been linked to increased risk of myocardial infarction, and a dense and protein-rich LDL has proved to be a characteristic of patients with manifest coronary heart disease (CHD). The present study focused on metabolic determinants of the LDL subfraction distribution with the emphasis placed on alimentary lipaemia. The relations of plasma levels and composition of light ($1.019 < d < 1.040 \text{ kg/l}$) and dense ($1.040 < d < 1.063 \text{ kg/l}$) LDL subfractions to postprandial triglyceride-rich lipoproteins (TGRL), postheparin plasma lipase activities and the activity of cholestrylo ester transfer protein (CETP)

were studied in 32 men with angiographically ascertained premature coronary atherosclerosis (age 48.8 ± 3.2 years) and in 10 age matched healthy control men. LDL subfractions were separated by equilibrium density gradient ultracentrifugation of fasting plasma drawn before participants were subjected to an oral fat tolerance test of a mixed meal type. The response of TGRL to the oral fat load was determined by measuring plasma triglycerides, and the apolipoprotein (apo) B-48 and apo B-100 content of Sf 60-400 and Sf 20-60 lipoprotein fractions. At a second visit plasma samples were taken for determination of postheparin plasma lipoprotein lipase (LPL) and hepatic lipase (HL) activities and for measurement of CETP activity. Hypertriglyceridaemic patients had a preponderance of dense LDL particles compared with normotriglyceridaemic patients and controls. The magnitude of the response of TGRL to the oral fat load showed a positive association with the dense LDL apo B concentration ($r = 0.32-0.52$, $P < 0.05$), whereas the LPL activity correlated positively with the free ($r = 0.50$, $P < 0.001$) and esterified cholesterol ($r = 0.45$, $P < 0.01$) and apo B ($r = 0.42$, $P < 0.01$) content of the light LDL fraction. The HL activity was found to be inversely associated with the plasma level of light LDL triglycerides ($r = -0.38$, $P < 0.05$). In contrast, no relations were noted between CETP activity and plasma concentrations of LDL constituents. Multiple stepwise linear regression analysis with the proportion of total LDL apo B contained in the dense LDL subfraction (% dense LDL apo B) used as the dependent variable indicated that the combined effect of LPL activity and postprandial plasma levels of TGRL (areas under the curve for plasma triglycerides or Sf 60-400 apo B-48) accounted for around 50% of the variability in the distribution of LDL particles between light and dense subfractions. (ABSTRACT TRUNCATED AT 400 WORDS)

... human low density lipoprotein: effects of postprandial triglyceride-rich lipoproteins, lipoprotein lipase, hepatic lipase and cholestrylo ester transfer protein.

Jan 4 1993,

A preponderance of small, dense low density lipoprotein (LDL) particles has been linked to increased risk of myocardial infarction, and a dense and protein-rich LDL has proved...

... subfractions to postprandial triglyceride-rich lipoproteins (TGRL),

postheparin plasma lipase activities and the activity of cholesteryl ester transfer protein (CETP) were studied in 32 men with angiographically ascertained premature coronary atherosclerosis (age 48.8 +/- 3...).

... of postheparin plasma lipoprotein lipase (LPL) and hepatic lipase (HL) activities and for measurement of CETP activity. Hypertriglyceridaemic patients had a preponderance of dense LDL particles compared with normotriglyceridaemic patients and...

... LDL triglycerides ($r = -0.38$, $P < 0.05$). In contrast, no relations were noted between CETP activity and plasma concentrations of LDL constituents. Multiple stepwise linear regression analysis with the proportion...

; Carrier Proteins--Blood--BL; Coronary Arteriosclerosis --Metabolism--ME; Dietary Fats--Metabolism--ME; Heparin--Pharmacology--PD; Lipoprotein...

Chemical Name: Lipase; (Lipoprotein Lipase; (cholesterol ester transfer proteins; (Carrier Proteins; (Dietary Fats; (Lipoproteins; (Lipoproteins, LDL; (Triglycerides; (Heparin

12/3, K, AB/26 (Item 26 from file: 155)
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07167931 93016858

Dietary cholesterol increases transcription of the human cholesteryl ester transfer protein gene in transgenic mice. Dependence on natural flanking sequences.

Jiang XC; Agellon LB; Walsh A; Breslow JL; Tall A
Department of Medicine, Columbia University, New York 10032.
J Clin Invest (UNITED STATES) Oct 1992, 90 (4) p1290-5, ISSN 0021-9738 Journal Code: HS7

Contract/Grant No.: HL-43165, HL, NHLBI; HL-21006, HL, NHLBI; HL-33714, HL, NHLBI; +

Languages: ENGLISH

Document type: JOURNAL ARTICLE

To investigate the regulation of expression of the human cholesteryl ester transfer protein (CETP) gene, transgenic mice were prepared using a CETP minigene linked to the natural flanking sequences of the human CETP gene. By using a transgene containing 3.2 kb of upstream and 2.0 kb of downstream flanking sequence, five different lines of transgenic mice were generated. The abundance of CETP mRNA in various tissues was determined on standard laboratory diet or high fat, high cholesterol diets. In three lines of transgenic mice the tissues expressing the human CETP mRNA were similar to those in humans (liver, spleen, small intestine, kidney, and adipose tissue); in two lines expression was more restricted. There was a marked (4-10-fold) induction of liver CETP mRNA in response to a high fat, high cholesterol diet. The increase in hepatic CETP mRNA was accompanied by a fivefold increase in transcription rate of the CETP transgene, and a 2.5-fold increase in plasma CETP mass and activity. In contrast, CETP transgenic mice, in which the CETP minigene was linked to a metallothionein promoter rather than to its own flanking sequences, showed no change in liver CETP mRNA in response to a high cholesterol diet. Thus (a) the CETP minigene or natural flanking sequences contain elements directing authentic tissue-specific expression; (b) a high cholesterol diet induces CETP transgene transcription, causing increased hepatic CETP mRNA and plasma CETP; (c) this cholesterol response requires DNA sequences contained in the natural flanking regions of the human CETP gene.

Dietary cholesterol increases transcription of the human

cholesteryl ester transfer protein gene in transgenic mice. Dependence on natural flanking sequences.

Oct 1992,

To investigate the regulation of expression of the human **cholesteryl ester transfer protein (CETP)** gene, transgenic mice were prepared using a **CETP** minigene linked to the natural flanking sequences of the human **CETP** gene. By using a transgene containing 3.2 kb of upstream and 2.0 kb of downstream flanking sequence, five different lines of transgenic mice were generated. The abundance of **CETP** mRNA in various tissues was determined on standard laboratory diet or high fat, high cholesterol diets. In three lines of transgenic mice the tissues expressing the human **CETP** mRNA were similar to those in humans (liver, spleen, small intestine, kidney, and adipose tissue...).

... lines expression was more restricted. There was a marked (4-10-fold) induction of liver **CETP** mRNA in response to a high fat, high cholesterol diet. The increase in hepatic **CETP** mRNA was accompanied by a fivefold increase in transcription rate of the **CETP** transgene, and a 2.5-fold increase in plasma **CETP** mass and activity. In contrast, **CETP** transgenic mice, in which the **CETP** minigene was linked to a metallothionein promoter rather than to its own flanking sequences, showed no change in liver **CETP** mRNA in response to a high cholesterol diet. Thus (a) the **CETP** minigene or natural flanking sequences contain elements directing authentic tissue-specific expression; (b) a high cholesterol diet induces **CETP** transgene transcription, causing increased hepatic **CETP** mRNA and plasma **CETP**; (c) this cholesterol response requires DNA sequences contained in the natural flanking regions of the human **CETP** gene.

Descriptors: **Carrier Proteins--Genetics--GE;** ***Cholesterol, Dietary--Pharmacology--PD;** ***Transcription, Genetic--Drug Effects--DE**

Chemical Name: **cholesterol ester transfer proteins; (Carrier Proteins; (Cholesterol, Dietary; (RNA, Messenger; (Metallothionein**

12/3, K, AB/27 (Item 27 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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06816974 92031355

Molecular cloning, sequence, and expression of cynomolgus monkey **cholesteryl ester transfer protein**. Inverse correlation between hepatic **cholesteryl ester transfer protein** mRNA levels and plasma high density lipoprotein levels.

Pape ME; Rehberg EF; Marotti KR; Melchior GW
Upjohn Company, Kalamazoo, Mich 49001.
Arterioscler Thromb (UNITED STATES) Nov-Dec 1991, 11 (6)
p1759-71, ISSN 1049-8834 Journal Code: AZ1

Languages: ENGLISH
Document type: JOURNAL ARTICLE
A cDNA clone containing the coding region for cynomolgus monkey **cholesteryl ester transfer protein (CETP)** was isolated by the polymerase chain reaction with primers based on the human **CETP** cDNA sequence and cDNA synthesized from liver poly (A+) RNA. Analysis of that cDNA indicated that the nucleotide and amino acid sequences of cynomolgus monkey **CETP** were greater than 95% homologous with the human sequences. A fragment of the cDNA was used to develop an internal-standard/RNase protection assay that allowed precise quantification of **CETP** mRNA levels. Analysis of total RNA from various tissues with this assay revealed that the liver and thoracic aorta expressed high levels of **CETP** mRNA; the mesenteric fat, adrenal gland, spleen, and abdominal aorta had low but detectable levels of the mRNA; and the brain, kidney, intestine, and skeletal muscle had undetectable levels of that mRNA. When the monkeys were made hypercholesterolemic by a high-fat, high-cholesterol (HFHC) diet, hepatic

levels of **CETP** mRNA increased from 1.6 +/- 0.4 pg/micrograms total RNA (mean +/- SEM) to 4.1 +/- 0.8 pg/micrograms (p less than 0.005); mesenteric fat **CETP** mRNA increased from 0.4 +/- 0.1 pg/micrograms total RNA to 5.3 +/- 2.2 pg/micrograms (p less than 0.05); and plasma CET activity increased approximately fourfold. The **CETP** mRNA levels in the thoracic and abdominal aortas were not significantly increased in monkeys fed the HFHC diet, even though those animals had gross atherosclerosis. The apoprotein E mRNA levels, however, were markedly increased in the aortas of monkeys with atherosclerosis, with the largest increase occurring in the abdominal aorta. Taken together, these data suggest that lipid deposition in the artery was not accompanied by increased expression of the **CETP** gene in that tissue. Statistical analysis showed that a strong, negative correlation existed between hepatic **CETP** mRNA levels and both high density lipoprotein cholesterol ($r = -0.85$, p less than 0.001) and apoprotein A-I ($r = -0.84$, p less than 0.001). These data suggest that HFHC diet-induced changes in high density lipoprotein metabolism may be linked to altered expression of a function **CETP** gene.

Molecular cloning, sequence, and expression of cynomolgus monkey **cholesteryl ester transfer protein**. Inverse correlation between hepatic **cholesteryl ester transfer protein** mRNA levels and plasma high density lipoprotein levels.

Nov-Dec 1991,

A cDNA clone containing the coding region for cynomolgus monkey **cholesteryl ester transfer protein** (**CETP**) was isolated by the polymerase chain reaction with primers based on the human **CETP** cDNA sequence and cDNA synthesized from liver poly (A+) RNA. Analysis of that cDNA indicated that the nucleotide and amino acid sequences of cynomolgus monkey **CETP** were greater than 95% homologous with the human sequences. A fragment of the cDNA was used to develop an internal-standard/RNase protection assay that allowed precise quantification of **CETP** mRNA levels. Analysis of total RNA from various tissues with this assay revealed that the liver and thoracic aorta expressed high levels of **CETP** mRNA; the mesenteric fat, adrenal gland, spleen, and abdominal aorta had low but detectable levels...

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... These data suggest that HFHC diet-induced changes in high density lipoprotein metabolism may be linked to altered expression of a function **CETP** gene.

Descriptors: **Carrier Proteins**--**Genetics**--GE; *Cloning, Molecular; *Lipoproteins, HDL--Blood--BL; *Liver--Metabolism--ME; **Macaca fascicularis*--**Genetics**...

Chemical Name: cholesterol ester transfer proteins; (**Carrier Proteins**; (Cholesterol, Dietary; (Dietary Fats; (Lipoproteins, HDL; (RNA, Messenger

06693451 91190902

Structure-function studies of human cholesteryl ester transfer protein by linker insertion scanning mutagenesis.

Wang S; Deng LP; Brown ML; Agellon LB; Tall AR
Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York 10032.

Biochemistry (UNITED STATES) Apr 9 1991, 30 (14) p3484-90,
ISSN 0006-2960 Journal Code: A0G

Contract/Grant No.: HL22682, HL, NHLBI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Human plasma cholesteryl ester transfer protein (**CETP**) enhances transfer and exchange of cholesteryl ester (CE) and triglyceride (TG) between high-density lipoprotein and other lipoproteins. To define regions responsible for the neutral lipid transfer activities at the molecular level, a total of 27 linker insertion mutants at 18 different sites along the **CETP** molecule were prepared and transiently expressed in a mammalian cell line (COS). The inserted linkers were small (usually 6 bp) and did not interrupt the translational reading frame of the **CETP** cDNA. Although secretion of each mutant protein was less than that of wild-type **CETP**, the majority of the mutants had normal cholesteryl ester transfer activity (transfer activity per nanogram of **CETP** in media). However, insertional alterations in three regions severely impaired CE transfer activity: (1) in the region of amino acids 48-53; (2) at amino acid 165; and (3) in the region of amino acids 373-379. Although the impaired activities could also be a result of globally incorrect folding of these **CETP** mutants, hydrophobicity analysis and secondary structure predictions tended to exclude this possibility for most of the insertion sites at which insertions resulted in inactivation. The insertion at amino acid 379 occurs immediately after a triplet of lysine residues, suggesting that this region might be involved in an essential step in the mechanism of CE and TG transfer, such as the binding of **CETP** to phosphatidylcholine molecules in the lipoprotein surface. Effects on TG transfer activity were generally similar to those on CE transfer activity, suggesting a similar structural requirement for both neutral lipid transfer activities.

Structure-function studies of human cholesteryl ester transfer protein by linker insertion scanning mutagenesis.

Apr 9 1991,

Human plasma cholesteryl ester transfer protein (**CETP**) enhances transfer and exchange of cholesteryl ester (CE) and triglyceride (TG) between high-density lipoprotein and other lipoproteins. To define regions responsible for the neutral lipid transfer activities at the molecular level, a total of 27 linker insertion mutants at 18 different sites along the **CETP** molecule were prepared and transiently expressed in a mammalian cell line (COS). The inserted linkers were small (usually 6 bp) and did not interrupt the translational reading frame of the **CETP** cDNA. Although secretion of each mutant protein was less than that of wild-type **CETP**, the majority of the mutants had normal cholesteryl ester transfer activity (transfer activity per nanogram of **CETP** in media). However, insertional alterations in three regions severely impaired CE transfer activity: (1) in...

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... essential step in the mechanism of CE and TG transfer, such as the binding of CETP to phosphatidylcholine molecules in the lipoprotein surface. Effects on TG transfer activity were generally similar...

Descriptors: Carrier Proteins--Genetics--GE; *Structure-Activity Relationship

Chemical Name: cholesterol ester transfer proteins; (Carrier Proteins; (Cholesterol Esters; (Triglycerides; (DNA

12/3, K, AB/29 (Item 29 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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06688476 91175821

Effects of various non-esterified fatty acids on the particle size redistribution of high density lipoproteins induced by the human cholesteroyl ester transfer protein.

Lagrost L; Barter PJ

Baker Medical Research Institute, Melbourne, Victoria, Australia.

Biochim Biophys Acta (NETHERLANDS) Mar 12 1991, 1082 (2) p204-10

, ISSN 0006-3002 Journal Code: AOW

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The effects of various non-esterified fatty acids on the CETP-mediated particle size redistribution of HDL were studied by incubating HDL3 and CETP for 24 h at 37 degrees C in the absence or in the presence of either saturated, monounsaturated or polyunsaturated non-esterified fatty acids. In the absence of non-esterified fatty acids, CETP induced a redistribution of the initial population of HDL3 (Stokes' radius 4.3 nm) by promoting the appearance of one larger (Stokes' radius 4.8 nm) and two smaller (Stokes' radii 3.9 and 3.7 nm) HDL subpopulations. Whereas the non-esterified fatty acids alone did not modify the HDL3 distribution profile, they were able to alter markedly the capacity of CETP to induce the particle size redistribution of HDL. All the saturated fatty acids with at least 10 carbons were able to increase the formation of the very small sized particles (Stokes' radius 3.7 nm) in a concentration dependent manner, the medium chain fatty acids (12 and 14 carbons) being the best activators. The potential effect of non-esterified fatty acids was also influenced by the presence of double bonds in their monomeric carbon chain. While at low concentrations of non-esterified fatty acids (0.1 mmol/l) the enhancement of the formation of very small HDL particles appeared to be greater with oleic and linoleic acids than with stearic acid, at higher concentrations (0.4 mmol/l), oleic, linoleic and arachidonic acids decreased the formation of the 3.7 nm radius particles. The inhibition of the process at high concentrations of unsaturated fatty acids was linked to the degree of unsaturation of their carbon chain, arachidonic acid being the strongest inhibitor. The present study has demonstrated that non-esterified fatty acids can modulate the particle size redistribution of HDL3 mediated by the cholesteroyl ester transfer protein even in the absence of any other lipoprotein classes. The effect of non-esterified fatty acid is dependent on both the length and the degree of unsaturation of their monomeric carbon chain.

... fatty acids on the particle size redistribution of high density lipoproteins induced by the human cholesteroyl ester transfer protein.

Mar 12 1991,

The effects of various non-esterified fatty acids on the CETP-mediated particle size redistribution of HDL were studied by incubating HDL3 and CETP for 24 h at 37 degrees C in the absence or in the presence of...

... monounsaturated or polyunsaturated non-esterified fatty acids. In the

absence of non-esterified fatty acids, CETP induced a redistribution of the initial population of HDL3 (Stokes' radius 4.3 nm) by...

... not modify the HDL3 distribution profile, they were able to alter markedly the capacity of CETP to induce the particle size redistribution of HDL. All the saturated fatty acids with at...

... radius particles. The inhibition of the process at high concentrations of unsaturated fatty acids was linked to the degree of unsaturation of their carbon chain, arachidonic acid being the strongest inhibitor...

...non-esterified fatty acids can modulate the particle size redistribution of HDL3 mediated by the **cholesteryl ester transfer protein** even in the absence of any other lipoprotein classes. The effect of non-esterified fatty...

Descriptors: **Carrier Proteins**--Pharmacology--PD; *Cholesterol Esters--Pharmacology--PD; *Fatty Acids, Nonesterified--Pharmacology--PD; *Lipoproteins, HDL--Blood...

Chemical Name: cholesterol ester transfer proteins; (**Carrier Proteins**; (Cholesterol Esters; (Fatty Acids, Nonesterified; (Lipoproteins, HDL

12/3, K, AB/30 (Item 30 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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06661013 90358924

Genetic variation in the **cholesteryl ester transfer protein** and apolipoprotein A-I genes and its relation to coronary heart disease in a Sri Lankan population.

Mendis S; Shepherd J; Packard CJ; Gaffney D
Department of Medicine, Faculty of Medicine, University of Peradeniya, Sri Lanka.

Atherosclerosis (NETHERLANDS) Jul 1990, 83 (1) p21-7, ISSN 0021-9150 Journal Code: 95X

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The influence of variation in the genes for **cholesteryl ester transfer protein** and apolipoprotein A-I was investigated in 95 patients with coronary heart disease and 95 matched control subjects of South East Asian extraction. Restriction fragment length polymorphisms (RFLPs) linked to the **cholesteryl ester transfer protein** gene TaqIA and TaqIB, and to the apolipoprotein A-I gene SstI, were examined to investigate the extent of genetic variation at these loci. None of the alleles defined by these RFLPs were associated with increased coronary risk. Analysis of the data by division of high density lipoprotein-cholesterol levels into tertiles showed a trend of a higher frequency of B1 allele (presence of the TaqIB site) with reduced high density lipoprotein levels. The B1 allele was more frequent in control subjects, with low high density lipoprotein levels (P less than 0.02), but not in coronary heart disease patients. The differences became significant for both groups (P less than 0.05) when the data of non-smokers were analysed separately.

Genetic variation in the **cholesteryl ester transfer protein** and apolipoprotein A-I genes and its relation to coronary heart disease in a Sri...

Jul 1990,
The influence of variation in the genes for **cholesteryl ester transfer protein** and apolipoprotein A-I was investigated in 95 patients with coronary heart disease and 95 matched control subjects of South East Asian extraction. Restriction fragment length polymorphisms (RFLPs) linked to the **cholesteryl ester transfer protein** gene TaqIA and TaqIB, and to the apolipoprotein A-I gene

SstI, were examined to...

Descriptors: Apolipoproteins A--Genetics--GE; *Carrier Proteins --Genetics--GE; *Coronary Disease--Genetics--GE
Chemical Name: cholesterol ester transfer proteins; (Apolipoprotein A-I; (Apolipoproteins A; (Carrier Proteins; (Lipoproteins, HDL Cholesterol; (Lipoproteins, VLDL; (Cholesterol

12/3,K,AB/31 (Item 31 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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06428599 90330670

A 70-kDa apolipoprotein designated ApoJ is a marker for subclasses of human plasma high density lipoproteins.

de Silva HV; Stuart WD; Duvic CR; Wetterau JR; Ray MJ; Ferguson DG; Albers HW; Smith WR; Harmony JA

Department of Pharmacology, University of Cincinnati, Ohio 45267.

J Biol Chem (UNITED STATES) Aug 5 1990, 265 (22) p13240-7,

ISSN 0021-9258 Journal Code: HIV

Contract/Grant No.: HL30999, HL, NHLBI; HL41496, HL, NHLBI; HL22619, HL, NHLBI; +

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A new apolipoprotein, termed apolipoprotein J (apoJ), was purified from human plasma by immunoaffinity chromatography. ApoJ is a glycoprotein consisting of disulfide-linked subunits of 34-36 and 36-39 kDa. Each subunit is glycosylated and has a PI range of 4.9-5.4. ApoJ exists in the plasma associated with high density lipoproteins (HDL) and specifically with subclasses of HDL which also contain apoAI and **cholesteryl ester transfer protein** activity. Immunoaffinity purified apoJ-HDL subclasses have apparent molecular masses of 80, 160, 240, 340, and 520 kDa, as determined by gradient gel electrophoresis. By negative staining electron microscopy, apoJ-HDL range in diameter from 5 to 16 nm. Fractionation of plasma by vertical gradient density centrifugation revealed apoJ-HDL in HDL2 (d 1.063-1.125 g/ml) with the majority overlapping HDL3 (d 1.125-1.21 g/ml) and very high density lipoprotein (d 1.21-1.25 g/ml). The bimodal density distribution of apoJ-HDL suggests that these subclasses have a unique metabolic relationship and may play a role in the transport of cholesterol from peripheral tissues to the liver.

Aug 5 1990,

... was purified from human plasma by immunoaffinity chromatography. ApoJ is a glycoprotein consisting of disulfide-linked subunits of 34-36 and 36-39 kDa. Each subunit is glycosylated and has a...

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; Antibodies, Monoclonal; Apolipoproteins--Isolation and Purification--IP ; Carrier Proteins--Blood--BL; Chromatography, Affinity; Electrophoresis, Gel, Two-Dimensional; Electrophoresis, Polyacrylamide Gel; Immunoblotting; Lipoproteins, HDL...

Chemical Name: cholesterol ester transfer proteins; (clusterin; (Antibodies, Monoclonal; (Apolipoproteins; (Biological Markers; (Carrier Proteins; (Lipoproteins, HDL

12/3,K,AB/32 (Item 32 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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06196585 88058996

Cholesteryl ester transfer protein is secreted by

Hep G2 cells and contains asparagine-linked carbohydrate and sialic acid.

Swenson TL; Simmons JS; Hesler CB; Bisgaier C; Tall AR

Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York 10032.

J Biol Chem (UNITED STATES) Dec 5 1987, 262 (34) p16271-4,
ISSN 0021-9258 Journal Code: HIV

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A cholesteryl ester transfer protein (CETP)

of apparent Mr 74,000 has recently been purified from human plasma. Cholesteryl ester transfer activity was found to accumulate in the medium of cultured Hep G2 cells. The transfer activity was removed by immunoprecipitation with specific antibodies to the plasma CETP. Sodium dodecyl sulfate gel electrophoresis of immunoprecipitates prepared from the medium of cells pulsed with [35S]methionine revealed a broad specific band of protein of Mr 72,000 to 76,000; by contrast, immunoprecipitates of cellular homogenates showed a sharp specific band of Mr 58,000. The Mr 72,000 to 76,000 band disappears, concomitant with the appearance of lower Mr products, upon neuraminidase or glycopeptidase F treatment of medium immunoprecipitates or of purified CETP. The results indicate that liver cells have the capacity to synthesize and secrete CETP. The CETP peptide acquires asparagine-linked carbohydrate and sialic acid during intracellular processing.

Cholesteryl ester transfer protein is secreted by Hep G2 cells and contains asparagine-linked carbohydrate and sialic acid.

Dec 5 1987,

A cholesteryl ester transfer protein (CETP)

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Descriptors: Asparagine--Analysis--AN; *Carbohydrates--Analysis--AN; *Carrier Proteins--Secretion--SE; *Liver Neoplasms, Experimental --Secretion--SE; *Sialic Acids--Analysis--AN

Chemical Name: Glycoside Hydrolases; (cholesterol ester transfer proteins ; (Carrier Proteins; (Sialic Acids; (N-Acetylneurameric Acid; (Asparagine

12/3,K,AB/33 (Item 1 from file: 34)
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci
(c) 1999 Inst for Sci Info. All rts. reserv.

06098237 Genuine Article#: XU911 Number of References: 134

Title: Intracellular cholesterol transport

Author(s): Fielding CJ (REPRINT) ; Fielding PE

Corporate Source: UNIV CALIF SAN FRANCISCO,CARDIOVASC RES INST/SAN

FRANCISCO//CA/94143 (REPRINT); UNIV CALIF SAN FRANCISCO,DEPT

PHYSIOL/SAN FRANCISCO//CA/94143; UNIV CALIF SAN FRANCISCO,DEPT MED/SAN

FRANCISCO//CA/94143

Journal: JOURNAL OF LIPID RESEARCH, 1997, V38, N8 (AUG), P1503-1521

ISSN: 0022-2275 Publication date: 19970800

Publisher: LIPID RESEARCH INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998

Language: English Document Type: REVIEW

Abstract: Recent data on the roles of vesicle- and 'raft'-mediated pathways in intracellular free cholesterol (FC) transport are reviewed. Cholesterol internalized from plasma lipoproteins is transferred via endocytic vesicles to the trans-Golgi network (TGN), consistent with prior data indicating a key role for this organelle in protein and lipid sorting and transport. Newly synthesized and lipoprotein-derived FC are returned to the cell surface by a common raft-dependent pathway. Intracellular FC transport promotes the delivery of GPI-anchored proteins to the cell surface; it is also an additional mechanism to regulate cell FC content. Many peripheral cells express caveolin, an FC-binding protein localized to plasma membrane caveolae. FC delivery to cell surface caveolae is accelerated by caveolin. Caveolar FC becomes targeted to small, lipid-poor (prebeta-) high density lipoprotein particles. Caveolin may protect quiescent cells, regulating FC efflux more efficiently in response to changing medium lipoprotein concentrations. Overall, these recent findings suggest that cell FC content can be regulated at the levels of both influx and efflux, and indicate key roles for the TGN and in cells expressing caveolin, cell-surface caveolae.

, 1997

...Identifiers--STEROL-CARRIER PROTEIN-2; HIGH-DENSITY-LIPOPROTEIN; ACYL-COENZYME-A; GLYCOSYLPHOSPHATIDYLINOSITOL-ANCHORED PROTEIN; RECEPTOR-MEDIATED ENDOCYTOSIS; RAT...

...Research Fronts: 2389 001 (MOLECULAR MECHANISMS IN SYNAPTIC VESICLE RECYCLING; NEUROTRANSMITTER RELEASE; BOTULINUM NEUROTOXIN POISONING; NEURONAL EXOCYTOTIC FUSION MACHINE)

95-3463 001 (CHOLESTERYL ESTER TRANSFER PROTEIN GENE; NATIVE PLASMA; DISTURBED HDL CONVERSION IN TANGIER DISEASE)

12/3, K, AB/34 (Item 2 from file: 34)
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci
(c) 1999 Inst for Sci Info. All rts. reserv.

05793245 Genuine Article#: WX814 Number of References: 46
Title: Iron-salicylate complex induces peroxidation, alters hepatic lipid profile and affects plasma lipoprotein composition

Author(s): Brunet S; Guertin F; Thibault L; Gavino V; Delvin E; Levy E (REPRINT)

Corporate Source: UNIV MONTREAL, HOP ST JUSTINE, PEDIAT RES CTR, DEPT NUTR, 3175 COTE ST CATHERINE/MONTREAL/PQ H3T 1C5/CANADA/ (REPRINT); UNIV MONTREAL, HOP ST JUSTINE, PEDIAT RES CTR, DEPT NUTR/MONTREAL/PQ H3T 1C5/CANADA/; UNIV MONTREAL, DEPT BIOCHEM/MONTREAL/PQ H3C 3J7/CANADA/

Journal: ATHEROSCLEROSIS, 1997, V129, N2 (MAR 21), P159-168

ISSN: 0021-9150 Publication date: 19970321

Publisher: ELSEVIER SCI IRELAND LTD, CUSTOMER RELATIONS MANAGER, BAY 15, SHANNON INDUSTRIAL ESTATE CO, CLARE, IRELAND

Language: English Document Type: ARTICLE

Abstract: Iron overload, with its associated toxic effects, has serious health consequences and results in damage to the liver, heart and other organs. Salicylate may be used as the lipophilic: carrier, transporting more iron into hepatocytes. In this study, we examined the effect of the combined administration of these compounds on plasma lipid profile and lipoprotein composition, as well as on hepatic lipid concentration. Male Sprague-Dawley rats were injected i.p. with Fe (15 mg/kg weight). This injection was repeated 24 h later with a gavage of sodium salicylate (700 mg/kg). Control rats received 0.9% NaCl only. The peroxidation indices TBARS ($P < 0.001$) and conjugated dienes ($P < 0.05$) significantly increased in the blood (50 and 122%, respectively) and liver (333 and 101%, respectively) of Fe-salicylate-treated rats. Concomitantly, blood and liver arachidonic acid content was diminished by iron treatment. In parallel, the plasma lipid profile was markedly affected in Fe-salicylate treated-rats.

Lower plasma concentrations of total cholesterol (25%, P < 0.0001) cholesteryl ester, (34%, P < 0.001) and high-density lipoprotein-cholesterol (50%, P < 0.001) were observed. Lipoprotein composition analysis revealed enrichment of free cholesterol and depletion of cholesterol ester in very low-density, intermediate-density low-density and high-density (HDL2, HDL3) lipoproteins. Furthermore, SDS-polyacrylamide gel electrophoresis revealed several alterations in the apolipoprotein distribution of these lipoproteins. The activity of lecithin:cholesterol acyltransferase was unchanged and could not account for the reduction of cholesterol esterification. As for the plasma, the liver exhibited a significant (P < 0.001) decrease in total cholesterol (2.42 +/- 0.07 versus 1.89 +/- 0.06 mg/g liver), essentially due to a reduction in cholesteryl ester (0.93 +/- 0.07 versus 0.51 +/- 0.03 mg/g liver, P < 0.001). Again, the activity of ACAT (dpm/mg microsomal protein) was not lower (12 700 +/- 1250) than that of controls (9650 +/- 1080). Thus, the iron-salicylate was able to induce peroxidation and to profoundly affect the intravascular and intrahepatic lipid, and plasma lipoprotein metabolism. Additional work is needed to elucidate the mechanisms involved in the underlying lipid and lipoprotein abnormalities. (C) 1997 Elsevier Science Ireland Ltd.

, 1997

...Abstract: damage to the liver, heart and other organs. Salicylate may be used as the lipophilic: carrier, transporting more iron into hepatocytes. In this study, we examined the effect of the combined...

...Control rats received 0.9% NaCl only. The peroxidation indices TBARS (P < 0.001) and conjugated dienes (P < 0.05) significantly increased in the blood (50 and 122%, respectively) and liver...

...Research Fronts: ENHANCED IN-VIVO LOW-DENSITY-LIPOPROTEIN OXIDATION; CORONARY ATHEROSCLEROSIS; ALPHA-TOCOPHEROL SUPPLEMENTATION)

95-3463 001 (CHOLESTERYL ESTER TRANSFER PROTEIN GENE; NATIVE PLASMA; DISTURBED HDL CONVERSION IN TANGIER DISEASE)

12/3, K, AB/35 (Item 3 from file: 34)
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci
(c) 1999 Inst for Sci Info. All rts. reserv.

04820405 Genuine Article#: UK467 Number of References: 42
Title: CONSTRUCTION AND FUNCTIONAL-CHARACTERIZATION OF RECOMBINANT FUSION PROTEINS OF HUMAN LIPOPROTEIN-LIPASE AND APOLIPOPROTEIN CII

Author(s): HOFFMANN MM; STOFFEL W
Corporate Source: JOSEPH STELZMANN STR 52/D-50931 COLOGNE//GERMANY//; UNIV COLOGNE, FAC MED, INST BIOCHEM/W-5000 COLOGNE//GERMANY//
Journal: EUROPEAN JOURNAL OF BIOCHEMISTRY, 1996, V237, N3 (MAY 1), P 545-552

ISSN: 0014-2956

Language: ENGLISH Document Type: ARTICLE

Abstract: The hydrolysis of triacylglycerols of chylomicrons and very low density lipoproteins by lipoprotein lipase (LPL) requires the presence of apolipoprotein (apo) CII as a cofactor. To obtain further information on the interaction of apo CII and LPL, we generated two fusion proteins consisting of the complete LPL molecule and the mature form of apo CII. The cDNAs of both proteins were either connected directly or by a segment encoding a 16-amino-acid linker peptide. The fused cDNAs were stably expressed in human embryonic kidney (HEK) 293 cells and the enzymic properties of the recombinant proteins were examined. The fusion proteins hydrolysed both emulsified long-chain (lipase) triacylglycerol substrate and a water-soluble short-chain (esterase) fatty acid ester substrate (p-nitrophenylbutyrate), regardless of whether or not they contained the linker peptide. In the absence of exogenous apo

CII, the fusion proteins had up to 3.5-times higher basal activity than wild-type LPL. Similar to wild-type LPL, the fusion proteins were inhibited by 1M NaCl, however less than wild-type LPL. A polyclonal antibody specific for apo CII impaired their ability to hydrolyse triacylglycerol emulsions. A similar effect was seen when the tetrapeptide KGEK was used as inhibitor, which corresponds to the carboxy-terminal four amino acids of apo CII.

Title: CONSTRUCTION AND FUNCTIONAL-CHARACTERIZATION OF RECOMBINANT FUSION PROTEINS OF HUMAN LIPOPROTEIN-LIPASE AND APOLIPOPROTEIN CII

, 1996

...Abstract: To obtain further information on the interaction of apo CII and LPL, we generated two fusion proteins consisting of the complete LPL molecule and the mature form of apo CII. The...

...both proteins were either connected directly or by a segment encoding a 16-amino-acid linker peptide. The fused cDNAs were stably expressed in human embryonic kidney (HEK) 293 cells and the enzymic properties of the recombinant proteins were examined. The fusion proteins hydrolysed both emulsified long-chain (lipase) triacylglycerol substrate and a water-soluble short-chain (esterase) fatty acid ester substrate (p-nitrophenylbutyrate), regardless of whether or not they contained the linker peptide. In the absence of exogenous apo CII, the fusion proteins had up to 3.5-times higher basal activity than wild-type LPL. Similar to wild-type LPL, the fusion proteins were inhibited by 1M NaCl, however less than wild-type LPL. A polyclonal antibody...

Research Fronts: 94-2778 002 (PANCREATIC LIPASE; ACTIVE-SITE SERINE; MALONYL COENZYME A-ACYL CARRIER PROTEIN TRANSACYLASE)
94-3070 002 (RAT SKELETAL-MUSCLE; DEVELOPMENTAL REGULATION; YEAST SACCHAROMYCES-CEREVISIAE)
94-2181...

...TYPE PLASMINOGEN-ACTIVATOR; ALTERED EXPRESSION)
94-2195 001 (LIPOPROTEIN-LIPASE ACTIVITY; DAHL SALT-SENSITIVE RATS; CHOLESTERYL ESTER TRANSFER PROTEIN TRANSGENIC MICE)

12/3, K, AB/36 (Item 4 from file: 34)
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci
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00874861 Genuine Article#: FD249 Number of References: 41
Title: CU2+-MEDIATED OXIDATION OF DIALYZED PLASMA - EFFECTS ON LOW AND HIGH-DENSITY-LIPOPROTEINS AND CHOLESTERYL ESTER TRANSFER PROTEIN

Author(s): ZAWADZKI Z; MILNE RW; MARCEL YL
Corporate Source: CLIN RES INST MONTREAL, LIPOPROT MED LAB, 110 PINE AVE W/MONTREAL H2W 1R7/QUEBEC/CANADA/; CLIN RES INST MONTREAL, LIPOPROT MED LAB, 110 PINE AVE W/MONTREAL H2W 1R7/QUEBEC/CANADA/

Journal: JOURNAL OF LIPID RESEARCH, 1991, V32, N2, P243-250

Language: ENGLISH Document Type: ARTICLE

Abstract: We previously reported that the expression of an epitope of apolipoprotein B (apoB), mapped to the C-terminus and defined by antibody B(sol)7, increased during Cu2+-mediated oxidation of isolated low density lipoprotein (LDL). We describe now the properties of B(sol)7 as a marker of LDL oxidation in whole plasma in relation to other effects of oxidative treatment of plasma, such as the distribution of apoA-I and cholesteryl ester transfer protein (CEPT). In dialyzed plasma, no LDL oxidation was detected at Cu2+ concentrations (5-mu-M) sufficient for extensive oxidation of isolated LDL. At a higher Cu2+ concentration (50-mu-M), an increased expression of the B(sol)7 epitope was observed; at

250-mu-M Cu²⁺, other evidence of LDL oxidation was found. The pattern of LDL response to Cu²⁺ observed in dialyzed plasma could be reproduced by adding 3% bovine serum albumin to isolated LDL. We demonstrate that the effect of albumin most likely results from its ability to bind copper ions. Incubation of plasma with increasing concentration of Cu²⁺ resulted first in the disappearance of alpha-2-migrating HDL, the usual carrier of CETP; free CETP and high molecular weight apoA-I-containing particles were also generated during oxidation. Addition of oxidized, but not native, LDL to plasma resulted in a transfer to LDL of some of the CETP initially associated with apoA-I.

In conclusion, the increased immunoreactivity of the B(sol)7 epitope was the most sensitive parameter of LDL oxidation, but other parameters, such as the presence of alpha-2-HDL and CETP-lipoprotein associations were even more sensitive evidence of lipoprotein oxidation.

Title: CU2+-MEDIATED OXIDATION OF DIALYZED PLASMA - EFFECTS ON LOW AND HIGH-DENSITY-LIPOPROTEINS AND CHOLESTERYL ESTER TRANSFER PROTEIN

, 1991

...Abstract: other effects of oxidative treatment of plasma, such as the distribution of apoA-I and cholesteryl ester transfer protein (CEPT). In dialyzed plasma, no LDL oxidation was detected at Cu²⁺ concentrations (5-mu-M...

...concentration of Cu²⁺ resulted first in the disappearance of alpha-2-migrating HDL, the usual carrier of CETP; free CETP and high molecular weight apoA-I-containing particles were also generated during oxidation. Addition of...

...not native, LDL to plasma resulted in a transfer to LDL of some of the CETP initially associated with apoA-I.

In conclusion, the increased immunoreactivity of the B(sol)7...

...of LDL oxidation, but other parameters, such as the presence of alpha-2-HDL and CETP-lipoprotein associations were even more sensitive evidence of lipoprotein oxidation.

...Research Fronts: LOW-DENSITY LIPOPROTEIN; MURINE MACROPHAGES; ROLE OF PLATELET SECRETORY PRODUCTS)

89-3034 002 (MICROTUBULE CROSS-LINKING PROTEIN; SMALL SYNAPTIC VESICLES OF RAT-BRAIN; AXOLININ LOCALIZATION)

? log off

07dec99 13:33:09 User231882 Session D487.3
\$9.48 3.159 DialUnits File155
\$0.40 2 Type(s) in Format 3 (UDF)
\$6.00 30 Type(s) in Format 4 (UDF)
\$6.40 32 Types
\$15.88 Estimated cost File155
\$1.94 0.369 DialUnits File55
\$1.94 Estimated cost File55
\$7.40 0.625 DialUnits File34
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\$9.00 3 Type(s) in Format 5 (UDF)
\$12.00 4 Types
\$19.40 Estimated cost File34
\$5.47 0.461 DialUnits File434
\$6.00 2 Type(s) in Format 3 (UDF)
\$6.00 2 Types
\$11.47 Estimated cost File434
OneSearch, 4 files, 4.614 DialUnits FileOS
\$0.60 TYMNET

\$49.29 Estimated cost this search
\$49.33 Estimated total session cost 4.812 DialUnits
Logoff: level 99.12.02 D 13:33:09

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? ds

Set      Items   Description
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S2       202     ANTIGENIC(5N)CARRIER
S3           1     S1 AND S2
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? s carrier
    S4 160083 CARRIER
? s s1 and s4
    547  S1
    160083 S4
    S5     46  S1 AND S4
? rd
...completed examining records
    S6     38  RD (unique items)
? s s6 and py<=1997
Processing
Processing
    38  S6
    28289569 PY<=1997
    S7     31  S6 AND PY<=1997
? s amino(w)termin?
    870664 AMINO
    597759 TERMIN?
    S8     46200 AMINO(W)TERMIN?
? s s7 and s8
    31  S7
    46200 S8
    S9     5   S7 AND S8
? t s9/3,k,ab/1-9

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9/3,K,AB/1 (Item 1 from file: 155)
 DIALOG(R) File 155: MEDLINE(R)
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12/9/99

07320611 92085371
 The position of heterologous epitopes inserted in hepatitis B virus core particles determines their immunogenicity [published erratum appears in J Virol 1992 Jun;66(6):3977]

Schodel F; Moriarty AM; Peterson DL; Zheng JA; Hughes JL; Will H; Leturcq DJ; McGee JS; Milich DR

Max-Planck-Institut fur Biochemie, Martinsried, Germany.
 J Virol (UNITED STATES) Jan 1992, 66 (1) p106-14, ISSN 0022-538X Journal Code: KCV

Contract/Grant No.: AI20720, AI, NIAID
 Languages: ENGLISH

Document type: JOURNAL ARTICLE

The nucleocapsid (HBcAg) of the hepatitis B virus (HBV) has been suggested as a carrier moiety for vaccine purposes. We investigated the influence of the position of the inserted epitope within hybrid HBcAg particles on antigenicity and immunogenicity. For this purpose, genes coding for neutralizing epitopes of the pre-S region of the HBV envelope proteins were inserted at the amino terminus, the amino terminus through a precore linker sequence, the truncated carboxy terminus, or an internal site of HBcAg by genetic engineering and were expressed in Escherichia coli. All purified hybrid HBc/pre-S polyproteins were particulate. Amino- and carboxy-terminal-modified hybrid HBc particles

retained HBcAg antigenicity and immunogenicity. In contrast, insertion of a pre-S(1) sequence between HBcAg residues 75 and 83 abrogated recognition of HBcAg by 5 of 6 anti-HBc monoclonal antibodies and diminished recognition by human polyclonal anti-HBc. Predictably, HBcAg-specific immunogenicity was also reduced. With respect to the inserted epitopes, a pre-S(1) epitope linked to the amino terminus of HBcAg was not surface accessible and not immunogenic. A pre-S(1) epitope fused to the amino terminus through a precore linker sequence was surface accessible and highly immunogenic. A carboxy-terminal-fused pre-S(2) sequence was also surface accessible but weakly immunogenic. Insertion of a pre-S(1) epitope at the internal site resulted in the most efficient anti-pre-S(1) antibody response. Furthermore, immunization with hybrid HBc/pre-S particles exclusively primed T-helper cells specific for HBcAg and not the inserted epitope. These results indicate that the position of the inserted B-cell epitope within HBcAg is critical to its immunogenicity.

Jan 1992,

The nucleocapsid (HBcAg) of the hepatitis B virus (HBV) has been suggested as a carrier moiety for vaccine purposes. We investigated the influence of the position of the inserted epitope...

... epitopes of the pre-S region of the HBV envelope proteins were inserted at the amino terminus, the amino terminus through a precore linker sequence, the truncated carboxy terminus, or an internal site of HBcAg...

... reduced. With respect to the inserted epitopes, a pre-S(1) epitope linked to the amino terminus of HBcAg was not surface accessible and not immunogenic. A pre-S(1) epitope fused to the amino terminus through a precore linker sequence was surface accessible and highly immunogenic. A carboxy-terminal-fused...

Chemical Name: presurface protein 1, hepatitis B surface antigen; (presurface protein 2, hepatitis B surface antigen; (DNA, Viral; (Epitopes; (Hepatitis B Antibodies; (Hepatitis B Core Antigens; (Hepatitis B Surface Antigens; (Protein Precursors; (Recombinant Fusion Proteins; (Viral Core Proteins

9/3, K, AB/2 (Item 2 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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06366267 90169850

Molecular characterization of a new variant of hepatitis B virus in a persistently infected homosexual man.

Bhat RA; Ulrich PP; Vyas GN

Department of Laboratory Medicine, University of California, San Francisco 94143-0100.

Hepatology (UNITED STATES) Feb 1990, 11 (2) p271-6, ISSN 0270-9139 Journal Code: GBZ

Contract/Grant No.: P01 HL-36589, HL, NHLBI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Based on the diversity of nucleotide sequences of cloned hepatitis B virus DNA genomes, we have predicted possible replication of genetic variants of human hepatitis B virus. This prediction is exemplified by studies of a chronic carrier of HBsAg/adw2, who lacked anti-HBc but carried exceedingly high levels of hepatitis B virus DNA in serum. Molecular characterization of a number of clones revealed a restriction map that deviated significantly from the typical pattern of the adw2 subtype, especially around the EcoRI site commonly used as a reference point. Mutations appearing consistently in the precore and core regions included (a) mutation in the precore region resulting in a termination codon after the initiation codon, (b) mutation of the core initiation codon and (c) an inframe insert of 36 nucleotides in the precore region with a new

initiation site for the core protein. The 36-nucleotide insertion resulted in a new core protein with 12 extra amino acids at its amino-terminal end. A few scattered point mutations were clustered in the amino-terminal half of the core gene. Although the core protein of this hepatitis B virus variant carried immunologically detectable HBcAg, the absence of a humoral immune response to HBcAg could have been caused by previous infection with human immunodeficiency virus. This naturally occurring human hepatitis B virus variant replicated efficiently without expressing the precore region, confirming previous observations made of the artificial mutants of duck hepatitis B virus.

Feb 1990,

...variants of human hepatitis B virus. This prediction is exemplified by studies of a chronic carrier of HBsAg/adw2, who lacked anti-HBc but carried exceedingly high levels of hepatitis B...

... nucleotide insertion resulted in a new core protein with 12 extra amino acids at its amino-terminal end. A few scattered point mutations were clustered in the amino-terminal half of the core gene. Although the core protein of this hepatitis B virus variant carried immunologically detectable HBcAg, the absence of a humoral immune response to HBcAg...

9/3,K,AB/3 (Item 1 from file: 55)
DIALOG(R) File 55:BIOSIS Previews(R)
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10811170 BIOSIS NO.: 199799432315
Expression of HIV-1 epitopes inserted into the nucleocapsid protein of human hepatitis B virus.
AUTHOR: Isaguliants M G(a); Kadoshnikov Yu P; Kalinina T I; Khudyakov Yu E; Semiletov Yu A; Smirnov V D; Wahren B
AUTHOR ADDRESS: (a)Ivanovsky Inst. Virol., Russian Acad. Med. Sci., ul. Gamalei 16, Moscow 123098**Russia
JOURNAL: Biochemistry (Moscow) 61 (3):p393-403 1996
ISSN: 0006-2979
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Hybrids of the core protein of hepatitis B virus (HBcAg)-5 were designed which carry N-terminal insertions of B- and T-cell epitopes of HIV-1: an immunodominant B-epitope from gp41, a T-cell epitope from p34 pol, and a cluster of B- and T-cell epitopes from p 17 gag. The hybrids were synthesized using two expression systems-one based on the thermoinducible PR promoter of bacteriophage lambda and the other based on THETA 10 promoter of bacteriophage T7, with 3-5 and 7-14% yields, respectively. The hybrids have dual HBV and HIV-1 immunospecificity and are assembled into particles similar to those formed by the protein carrier HBcAg. Sandwich ELISA and immune electron microscopy revealed that the HIV-1 epitopes are exposed on the surface of the particles.

ABSTRACT: Hybrids of the core protein of hepatitis B virus (HBcAg)-5 were designed which carry N-terminal insertions of B- and T-cell...

...HIV-1 immunospecificity and are assembled into particles similar to those formed by the protein carrier HBcAg. Sandwich ELISA and immune electron microscopy revealed that the HIV-1 epitopes are exposed ...

MISCELLANEOUS TERMS: . . . AMINO-TERMINAL INSERTIONS
1996

9/3,K,AB/4 (Item 1 from file: 34)
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci
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05526097 Genuine Article#: WE313 Number of References: 22
Title: Expression of a human cytomegalovirus gp58 antigenic domain fused to
the hepatitis B virus nucleocapsid protein
Author(s): Tarar MR; Emery VC; Harrison TJ (REPRINT)
Corporate Source: UNIV LONDON, ROYAL FREE HOSP, SCH MED, DEPT MED, ROWLAND
HILL ST/LONDON NW3 2PF//ENGLAND/ (REPRINT); UNIV LONDON, ROYAL FREE
HOSP, SCH MED, DEPT MED/LONDON NW3 2PF//ENGLAND/; UNIV LONDON, ROYAL
FREE HOSP, SCH MED, DEPT VIROL/LONDON NW3 2PF//ENGLAND/
Journal: FEMS IMMUNOLOGY AND MEDICAL MICROBIOLOGY, 1996, V16, N3-4 (12/9/99)
DEC 31), P183-192
ISSN: 0928-8244 Publication date: 19961231
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
Language: English Document Type: ARTICLE
Abstract: Hepatitis B virus core antigen (HBcAg) has been used as a
carrier for expression and presentation of a variety of
heterologous viral epitopes in particulate form. The aim of this study
was to produce hybrid antigens comprising HBcAg and an immunogenic
epitope of human cytomegalovirus (HCMV). A direct comparison was made
of amino and carboxyl terminal fusions in order to investigate the
influence of position of the foreign epitope on hybrid core particle
formation, antigenicity and immunogenicity. HCMV DNA encoding a
neutralising epitope of the surface glycoprotein gp58 was either
inserted at the amino terminus or fused to the truncated
carboxyl terminus of HBcAg and expressed in Escherichia coli. The
carboxyl terminal fusion (HBc(3-144)-HCMV) was expressed at high levels
and assembled into core like particles resembling native HBcAg. Protein
with a similar fusion at the amino terminus
(HCMV-HBc(1-183)) could not be purified or characterised
immunologically, although it formed core like particles.
HBc(3-144)-HCMV displayed HBc antigenicity but HCMV antigenicity could
not be detected by radioimmunoassay or western blotting using anti-HCMV
monoclonal antibody 7-17 or an anti-HCMV human polyclonal antiserum.
Following immunisation of rabbits with HBc(3-144)-HCMV, a high titre of
anti-HBc specific antibody was produced along with lower titres of
HCMV/gp58 specific antibody.

, 1996

Abstract: Hepatitis B virus core antigen (HBcAg) has been used as a
carrier for expression and presentation of a variety of
heterologous viral epitopes in particulate form. The...

...DNA encoding a neutralising epitope of the surface glycoprotein gp58 was
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truncated carboxyl terminus of HBcAg and expressed in Escherichia coli.
The carboxyl...

...assembled into core like particles resembling native HBcAg. Protein with
a similar fusion at the amino terminus (HCMV-HBc(1-183))
could not be purified or characterised immunologically, although it
formed core...

9/3,K,AB/5 (Item 2 from file: 34)
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci
(c) 1999 Inst for Sci Info. All rts. reserv.

01576210 Genuine Article#: HJ504 Number of References: 39
Title: ASSEMBLY OF HEPATITIS-DELTA VIRUS-PARTICLES
Author(s): RYU WS; BAYER M; TAYLOR J

Corporate Source: FOX CHASE CANC INST, 7701 BURHOLME
AVE/PHILADELPHIA//PA/19111; FOX CHASE CANC INST, 7701 BURHOLME
AVE/PHILADELPHIA//PA/19111

Journal: JOURNAL OF VIROLOGY, 1992, V66, N4 (APR), P2310-2315

Language: ENGLISH Document Type: ARTICLE

Abstract: Hepatitis delta virus (HDV) is a subviral satellite of hepatitis B virus (HBV). Since the RNA genome of HDV can replicate in cultured cells in the absence of HBV, it has been suggested that the only helper function of HBV is to supply HBV coat proteins in the assembly process of HDV particles. To examine the factors involved in such virion assembly, we transiently cotransfected cells with various hepadnavirus constructs and cDNAs of HDV and analyzed the particles released into the medium. We report that the HDV genomic RNA and the delta antigen can be packaged by coat proteins of either HBV or the related hepadnavirus woodchuck hepatitis virus (WHV). Among the three co-carboxy-terminal coat proteins of WHV, the smallest form was sufficient to package the HDV genome; even in the absence of HDV RNA, the delta antigen could be packaged by this WHV coat protein. Also, of the two co-amino-terminal forms of the delta antigen, only the larger form was essential for packaging.

, 1992

...Abstract: delta antigen could be packaged by this WHV coat protein.
Also, of the two co-amino-terminal forms of the delta antigen, only the larger form was essential for packaging.

...Identifiers--B SURFACE-ANTIGEN; CARRIER CHIMPANZEE; RNA; GENOME; LIVER; SERUM; AGENT; DNA; REPLICATION; WOODCHUCK

...Research Fronts: B VIRUS; ANTI-HBX ANTIBODIES DETECTION IN CHRONIC HBV INFECTION; UPSTREAM AUG CODON FOR THE CORE PROTEIN)

90-0266 001 (EXPRESSION OF THE HEPATITIS-B VIRUS SURFACE-ANTIGEN GENE; HEPATOMA-CELL LINES INVITRO; INTERLEUKIN-6 RESPONSE ELEMENTS)

90-0693 001...

9/3,K,AB/5 (Item 5 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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05573301 89292152

Monoclonal antibody inhibition of cholesteryl ester transfer protein activity in the rabbit. Effects on lipoprotein composition and high density lipoprotein cholesteryl ester metabolism.
Whitlock ME; Swenson TL; Ramakrishnan R; Leonard MT; Marcel YL; Milne RW; Tall AR

Department of Medicine, Columbia University College of Physicians & Surgeons, New York 10032.

J Clin Invest (UNITED STATES) Jul 1989, 84 (1) p129-37, ISSN 0021-9738 Journal Code: HS7

Contract/Grant No.: HL-21006, HL, NHLBI; HL-22682, HL, NHLBI; T-07343
Languages: ENGLISH

Document type: JOURNAL ARTICLE

Cholesteryl ester transfer protein (CETP)
promotes in vitro transfer of cholesteryl ester (CE) and triglyceride (TG) between lipoproteins. We studied the function of CETP in vivo in rabbit lipoprotein metabolism using a neutralizing monoclonal antibody (MAb, TP1) to CETP. Rabbits were injected with TP1 (n = 8), or irrelevant MAb or saline (control, n = 8), resulting in an initial 71% inhibition of CETP, which fell to 45% after 48 h. HDL CE rose in the inhibited animals, reaching levels that doubled initial and control values at 48 h (P less than 0.001). HDL TG fell reciprocally, but HDL protein did not change, suggesting a CE for TG exchange. VLDL CE/TG decreased. Rabbits were also given [3H]cholesteryl ether HDL (a CE analogue). CETP inhibition delayed the initial clearance of radioactivity from HDL (control 6.8 vs. TP1 4.1 pools/d) and plasma (7.8 vs. 5.2 pools/d). We conclude that CETP plays a quantitatively important role in HDL CE catabolism in the rabbit, promoting the exchange of TG for CE and the

12/9/99

08085429 95105666

Inhibition of cholesteryl ester transfer protein
in normocholesterolemic and hypercholesterolemic hamsters: effects on
HDL subspecies, quantity, and apolipoprotein distribution.

Evans GF; Bensch WR; Apelgren LD; Bailey D; Kauffman RF; Bumol TF;
Zuckerman SH

Division of Cardiovascular Research, Lilly Research Labs, Lilly Corporate
Center, Indianapolis, IN 46285.

J Lipid Res (UNITED STATES) Sep 1994, 35 (9) p1634-45, ISSN
0022-2275 Journal Code: IX3

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The effects of cholesteryl ester transfer protein (CETP) inhibition on the serum lipoprotein profile in both normocholesterolemic and hypercholesterolemic hamsters has been determined following subcutaneous injection of 12.5 mg/kg of the CETP neutralizing monoclonal antibody, TP2. Inhibition of CETP activity was greater than 60% and resulted in a 30-40% increase in high density lipoprotein (HDL) in both normal and hypercholesterolemic animals. These HDL effects were observed 1 day post-injection, were maximal by 4 days, and returned to control values by 14 days. Inhibition of CETP activity resulted in a decrease in both low density lipoprotein (LDL) and very low density lipoprotein (VLDL) cholesterol concomitant with HDL increase, and in hypercholesterolemic animals resulted in increased total serum cholesterol. In addition to the quantitative differences in LDL and HDL, there were significant increases in the size of the HDL, a shift to smaller LDL particles, and changes in apolipoprotein (apo) composition as evaluated by FPLC and Western blot analysis. Large apoA-I-poor and apoE-containing HDL became prevalent in hypercholesterolemic hamsters after CETP inhibition. In addition, the size of the CETP-containing HDL particles increased with inhibition of transfer activity. While these effects were apparent in normocholesterolemic animals, the changes in apolipoprotein distribution and HDL subspecies as detected on native gels were more significant in the hypercholesterolemic animals. The changes in the HDL profile and apolipoprotein distribution after CETP inhibition in hamsters were similar to those reported in CETP-deficient Japanese subjects, suggesting the utility of the hypercholesterolemic hamster as an in vivo model for the understanding of the lipoprotein changes associated with CETP inhibition.

9/3,K,AB/3 (Item 3 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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08117120 95160779

Inhibition of **cholesteryl ester transfer protein**
activity in hamsters alters **HDL** lipid composition.

Gaynor BJ; Sand T; Clark RW; Aiello RJ; Bamberger MJ; Moberly JB

Department of Cardiovascular and Metabolic Diseases, Pfizer, Inc.,
Groton, CT 06340.

Atherosclerosis (IRELAND) Sep 30 1994, 110 (1) p101-9, ISSN
0021-9150 Journal Code: 95X

Languages: ENGLISH

Document type: JOURNAL ARTICLE

We investigated the role of **cholesteryl ester transfer protein** (**CETP**) in hamsters by using a monoclonal antibody (MAb) that inhibited hamster **CETP** activity. MAbs were prepared against partially purified human **CETP** and screened for inhibition of ³H-cholesteryl oleate (CE) transfer from LDL to **HDL** in the presence of human plasma bottom fraction ($d > 1.21$ g/ml). Antibody 1C4 inhibited CE transfer activity in both human plasma bottom fraction (IC_{50} = approximately 4 micrograms/ml) and in whole plasma from male Golden Syrian hamsters (IC_{50} = approximately 30 micrograms/ml). Purified MAb 1C4 was injected into chow- and cholesterol-fed hamsters, and blood was collected for analysis of plasma **CETP** activity and **HDL** lipid composition. Plasma **CETP** activity was inhibited by 70%-80% at all times up to 24 h following injection of 500 micrograms MAb 1C4 (approximately 3.7 mg/kg). The amount of antibody required for 50% inhibition at 24 h post-injection was 200 micrograms (approximately 1.5 mg/kg). Inhibition of hamster **CETP** activity in vivo increased hamster **HDL** cholesterol by 33% ($P < 0.0001$), increased **HDL**-CE by 31% ($P < 0.0001$) and decreased **HDL**-triglyceride by 42% ($P < 0.0001$) ($n = 36$) as determined following isolation of **HDL** by ultracentrifugation. An increase in **HDL** cholesterol and a redistribution of cholesterol to a larger **HDL** particle were also observed following fast protein liquid chromatography (FPLC) gel filtration of plasma lipoproteins. (ABSTRACT TRUNCATED AT 250 WORDS)

9/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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08361112 95333876

Cholesteryl ester transfer protein inhibition in hypercholesterolemic hamsters: kinetics of apoprotein changes.

Zuckerman SH; Evans GF

Division of Cardiovascular Research, Lilly Research Labs, Indianapolis, Indiana 46285, USA.

Lipids (UNITED STATES) Apr 1995, 30 (4) p307-11, ISSN 0024-4201
Journal Code: L73

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Inhibition of cholesteryl ester transfer protein (CETP) activity in hypercholesterolemic hamsters results in elevated high-density lipoprotein (HDL) cholesterol, an increase in HDL size, and the appearance of apolipoprotein E (apo E)-rich, apo A-I-poor particles. The present study has focused on the kinetics of apoprotein redistribution among the HDL particles and the relative increase in HDL-associated apo E and CETP in hypercholesterolemic hamsters, following inhibition of transfer activity using the monoclonal antibody, TP2. A 60% inhibition in CETP activity was observed 24 h after antibody injection and was associated with an increase in HDL cholesterol and HDL size. Increased amounts of apo E were associated with these HDL particles and remained in this fraction throughout the duration of the study. In contrast, while CETP was also detected on large HDL particles, this distribution shifted back toward the pretreatment pattern by 14 d. The dynamic changes in apoprotein distribution may represent a compensatory physiologic response following disruption of reverse cholesterol transport.

Cholesteryl ester transfer protein inhibition in hypercholesterolemic hamsters: kinetics of apoprotein changes.

Apr 1995,

Inhibition of cholesteryl ester transfer protein

? s cholesteryl(w)ester(5n)transfer(5n)protein or cetp
14593 CHOLESTERYL
146116 ESTER
510372 TRANSFER
2255487 PROTEIN
2718 CHOLESTERYL (W) ESTER (5N) TRANSFER (5N) PROTEIN
1558 CETP
S1 2955 CHOLESTERYL (W) ESTER (5N) TRANSFER (5N) PROTEIN OR CETP
? s hdl

S2 43287 HDL
? s s1 and s2

2955 S1
43287 S2
S3 1907 S1 AND S2
? s immuniz? or inject?

138440 IMMUNIZ?
666431 INJECT?
S4 786457 IMMUNIZ? OR INJECT?
? s s3 and s4

1907 S3
786457 S4
S5 85 S3 AND S4
? s s5 and py<=1997

Processing
Processing
85 S5
28289569 PY<=1997
S6 67 S5 AND PY<=1997
? rd

...examined 50 records (50)
...completed examining records
S7 49 RD (unique items)
? s antibod?

S8 1095515 ANTIBOD?
? s s7 and s8

49 S7
1095515 S8
S9 10 S7 AND S8
? t s9/3,k,ab/1-10

9/3,K,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155: MEDLINE(R)
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09270886 97338192
Cholesteryl ester transfer protein activity
enhances plasma cholesteryl ester formation. Studies in
CETP transgenic mice and human genetic CETP deficiency.

Oliveira HC; Ma L; Milne R; Marcovina SM; Inazu A; Mabuchi H; Tall AR
Department of Medicine, Columbia University, New York, NY 10032, USA.
Arterioscler Thromb Vasc Biol (UNITED STATES) Jun 1997, 17 (6)
p1045-52, ISSN 1079-5642 Journal Code: B89

Contract/Grant No.: HL-54591, HL, NHLBI; HL-22682, HL, NHLBI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The plasma cholesteryl ester transfer protein (**CETP**) promotes the removal of HDL cholesteryl esters and is thought to stimulate reverse cholesterol transport (RCT). However, mechanisms by which **CETP** may stimulate RCT are poorly understood. Thus, we examined the relationship between plasma **CETP** expression and plasma cholesteryl ester formation in **CETP** transgenic (Tg) mice, hamsters, and human subjects with genetic **CETP** deficiency. Incubation of **CETP** Tg mouse plasma showed a 20% to 40% increase in plasma cholesterol esterification rate (CER, $P < .05$) compared with control mice.

Injection of a neutralizing CETP monoclonal antibody

(MAb) (TP2) into natural flanking region **CETP** Tg mice resulted in an increase in plasma free cholesterol (FC) concentration, FC/CE ratio, FC/phosphatidylcholine ratio, and hepatic **CETP** mRNA. In hamsters, **CETP** inhibition also resulted in an increase in plasma FC/phosphatidylcholine ratio and increased **CETP** mRNA in adipose tissue. In humans with two common **CETP** gene mutations (an intron 14 splicing defect and a D442G missense mutation), mean plasma CERs were 39 and 60, respectively, compared with $89 \text{ nmol} \times \text{mL}^{-1} \times \text{h}^{-1}$ in normal subjects. By contrast, lecithin:cholesterol acyltransferase (LCAT) mass was normal in **CETP**-deficient subjects. MAb neutralization of **CETP** activity in incubated human plasma did not alter the LCAT reaction, even after supplementation with discoidal HDL and VLDL. Thus, genetic alterations in **CETP** levels lead to secondary changes in the plasma LCAT reaction, possibly because of remodeling of HDL by **CETP** acting in concert with other factors *in vivo*. In human genetic **CETP** deficiency, a moderate impairment in the plasma LCAT reaction may contribute to a defect in RCT, providing a potential mechanism to explain the recently observed excess of coronary heart disease in these subjects.

Cholesteryl ester transfer protein activity enhances plasma cholesteryl ester formation. Studies in CETP transgenic mice and human genetic CETP deficiency.

Jun 1997,

The plasma cholesteryl ester transfer protein (**CETP**) promotes the removal of HDL cholesteryl esters and is thought to stimulate reverse cholesterol transport (RCT). However, mechanisms by which **CETP** may stimulate RCT are poorly understood. Thus, we examined the relationship between plasma **CETP** expression and plasma cholesteryl ester formation in **CETP** transgenic (Tg) mice, hamsters, and human subjects with genetic **CETP** deficiency. Incubation of **CETP** Tg mouse plasma showed a 20% to 40% increase in plasma cholesterol esterification rate (CER, $P < .05$) compared with control mice.

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... h^{-1} in normal subjects. By contrast, lecithin:cholesterol acyltransferase (LCAT) mass was normal in **CETP**-deficient subjects. MAb neutralization of **CETP** activity in incubated human plasma did not alter the LCAT reaction, even after supplementation with discoidal HDL and VLDL. Thus, genetic alterations in **CETP** levels lead to secondary changes in the plasma LCAT reaction, possibly because of remodeling of HDL by **CETP** acting in concert with other factors

in vivo. In human genetic CETP deficiency, a moderate impairment in the plasma LCAT reaction may contribute to a defect in...

9/3,K,AB/2 (Item 2 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

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08361112 95333876

Cholesteryl ester transfer protein inhibition in hypercholesterolemic hamsters: kinetics of apoprotein changes.

Zuckerman SH; Evans GF

Division of Cardiovascular Research, Lilly Research Labs, Indianapolis, Indiana 46285, USA.

Lipids (UNITED STATES) Apr 1995, 30 (4) p307-11, ISSN 0024-4201
Journal Code: L73

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Inhibition of **cholesteryl ester transfer protein (CETP)** activity in hypercholesterolemic hamsters results in elevated

SYSTEM:OS - DIALOG OneSearch
 File 155: MEDLINE(R) 1966-1999/Dec W4
 (c) format only 1999 Dialog Corporation
 *File 155: Medline updates are complete for 1999.
 First update for 2000 will be added in mid-December.
 File 55: BIOSIS Previews(R) 1993-1999/Oct W5
 (c) 1999 BIOSIS
 File 34: SciSearch(R) Cited Ref Sci 1990-1999/Nov W4
 (c) 1999 Inst for Sci Info
 File 434: SciSearch(R) Cited Ref Sci 1974-1989/Dec
 (c) 1998 Inst for Sci Info

Set	Items	Description

? s	cetp or cholesteryl(w)ester(5n)transfer(5n)protein	
	1558	CETP
	14593	CHOLESTERYL
	146116	ESTER
	510372	TRANSFER
	2255487	PROTEIN
	2718	CHOLESTERYL(W)ESTER(5N)TRANSFER(5N)PROTEIN
S1	2955	CETP OR CHOLESTERYL(W)ESTER(5N)TRANSFER(5N)PROTEIN
? s	hbcag or hepatitis(w)B(5n)core(5n)protein	
	1422	HBCAG
	197390	HEPATITIS
	1308061	B
	181258	CORE
	2255487	PROTEIN
	547	HEPATITIS(W)B(5N)CORE(5N)PROTEIN
S2	1849	HBCAG OR HEPATITIS(W)B(5N)CORE(5N)PROTEIN
? s	s1 and s2	
	2955	S1
	1849	S2
S3	0	S1 AND S2
? s	hepatitis(w)b	
	197390	HEPATITIS
	1308061	B
S4	80897	HEPATITIS(W)B
? s	s1 and s4	
	2955	S1
	80897	S4
S5	2	S1 AND S4
? rd		
...completed examining records		
S6	2	RD (unique items)
? t	s6/3,k,ab/1-2	

6/3,K,AB/1 (Item 1 from file: 434)
 DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
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09404686 Genuine Article#: U1127 Number of References: 39

Title: MECHANISM OF THE CHOLESTERYL ESTER TRANSFER
PROTEIN-MEDIATED UPTAKE OF HIGH-DENSITY LIPOPROTEIN CHOLESTERYL
ESTERS BY HEP G2 CELLS
Author(s): RINNINGER F; PITTMAN RC
Corporate Source: UNIV CALIF SAN DIEGO, DEPT MED/LA JOLLA//CA/92093
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 1989, V264, N11, P6111-6118
Language: ENGLISH Document Type: ARTICLE

Title: MECHANISM OF THE CHOLESTERYL ESTER TRANSFER
PROTEIN-MEDIATED UPTAKE OF HIGH-DENSITY LIPOPROTEIN CHOLESTERYL
ESTERS BY HEP G2 CELLS
...Research Fronts: CORONARY HEART-DISEASE)
87-0251 001 (HUMAN HEPATOMA-CELL LINE HEPG2; ACUTE PHASE
PLASMA-PROTEINS; HEPATITIS-B VIRUS INVITRO)
87-3127 001 (CALCIUM-BINDING PROTEIN; TISSUE LOCALIZATION;
ESCHERICHIA-COLI GENE; PROGESTERONE-RECEPTOR...)

6/3,K,AB/2 (Item 2 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
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08143294 Genuine Article#: H6819 Number of References: 36
Title: SYNTHESIS AND SECRETION OF PLASMA CHOLESTERYL ESTER
TRANSFER PROTEIN BY HUMAN HEPATO-CARCINOMA CELL-LINE, HEPG2
Author(s): FAUST RA; ALBERS JJ
Corporate Source: UNIV WASHINGTON, SCH MED, DEPT PATHOL/SEATTLE//WA/98104;
UNIV WASHINGTON, SCH MED, DEPT MED/SEATTLE//WA/98104; NW LIPID RES
CLIN/SEATTLE//WA/98104
Journal: ARTERIOSCLEROSIS, 1987, V7, N3, P267-275
Language: ENGLISH Document Type: ARTICLE

Title: SYNTHESIS AND SECRETION OF PLASMA CHOLESTERYL ESTER
TRANSFER PROTEIN BY HUMAN HEPATO-CARCINOMA CELL-LINE, HEPG2
Research Fronts: 86-0242 001 (HUMAN HEPATOMA-CELL LINE HEPG2;
HEPATITIS-B VIRUS; LOW-DENSITY LIPOPROTEINS METABOLISM; RAT
HEPATOMA-CELLS; CLONED CDNA)
86-0459 001 (LOW-DENSITY...)



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Indexing Officer: JFUNSTEN - JAMES FUNSTEN

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Dossier: 09387340

Legal Date: 12-09-1999

No.	Doccode	Number of pages
1	SRNT	10
2	SRNT	12

Total number of pages: 22

Remarks:

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